Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US2005/010912

International filing date: 31 March 2005 (31.03.2005)

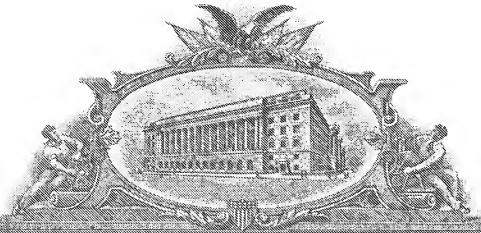
Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/559,202
Filing date: 01 April 2004 (01.04.2004)

Date of receipt at the International Bureau: 12 August 2005 (12.08.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)

World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse



1387289

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

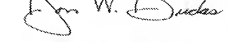
United States Patent and Trademark Office

August 02, 2005

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: ***60/559,202***
FILING DATE: ***April 01, 2004***
RELATED PCT APPLICATION NUMBER: ***PCT/US05/10912***

Certified by



Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office

PTO/SB/16 (08-03)
Approved for use through 7/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. EL 961008121 US

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Steven	MAH	San Diego, California
Andreas	BRAUN	San Diego, California
Stefan M.	KAMMERER	San Diego, California

Additional inventors are being named on the 1 *separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

METHODS FOR IDENTIFYING RISK OF OSTEOARTHRITIS AND TREATMENTS THEREOF

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

[x] Customer Number: 25225

OR

[ ] Firm or Individual Name

Address

City | State | Zip

Country | Telephone | Fax

ENCLOSED APPLICATION PARTS (*check all that apply*)

[x] Specification *Number of Pages* 240 [ ] CD(s), Number

[x] Drawing(s) *Number of Sheets* 2 [x] Other (specify): Return Receipt Postcard

[x] Application Data Sheet. See 37 CFR 1.76 (4 pages)

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

[x] Applicant claims small entity status. See 37 CFR 1.27.

[ ] A check or money order is enclosed to cover the filing fees.

[x] The Director is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 03-1952

[ ] Payment by credit card. Form PTO-2038 is attached.

FILING FEE AMOUNT ($): 80.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

[x] No [ ] Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

SIGNATURE

TYPED OR PRINTED NAME Bruce D. Grant

TELEPHONE (858) 720-7962

Date April 1, 2004

REGISTRATION NO. *(if appropriate)* 47,608

Docket Number: 524593008700

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EL 961008121 US, in an envelope addressed to: Mail Stop Provisional Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: 4/1/04 Signature: (Deborah Wykes)

PROVISIONAL APPLICATION COVER SHEET
Additional Page

PTO/SB/16 (08-03)
Approved for use through 07/31/06. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Docket Number 52459300870O

INVENTOR(S)/APPLICANT(S)

Given Name (first and middle [if any])	Family or Surname	Residence (City and either State or Foreign Country)
Matthew Roberts	NELSON	San Marcos, California
Rikard Henry	RENELAND	San Diego, California
Maria L.	LANGDOWN	San Diego, California

sd-189429

METHODS FOR IDENTIFYING RISK OF OSTEOARTHRITIS AND TREATMENTS THEREOF

Field of the Invention

[0001] The invention relates to genetic methods for identifying risk of osteoarthritis and treatments that specifically target such diseases.

Background

[0002] Osteoarthritis (OA) is a chronic disease usually affecting weight-bearing synovial joints. There are approximately 20 million Americans affected by OA and it is the leading cause of disability in the United States. In addition to extensive human suffering, OA also accounts for nearly all knee replacements and more than half of all hip replacements in the United States. Despite its prevalence, OA is poorly understood and there are few treatments available besides anti-inflammatory drugs and joint replacement.

[0003] Most commonly affecting middle-aged and older people, OA can range from very mild to very severe. It affects hands and weight-bearing joints such as knees, hips, feet and the back. Knee OA can be as disabling as any cardiovascular disease except stroke.

[0004] OA is characterized by the breakdown of cartilage in joints. Cartilage in joints cushions the ends of bones, and cartilage breakdown causes bones to rub against each other, causing pain and loss of movement. Type II collagen is the main component of cartilage, comprising 15-25% of the wet weight, approximately half the dry weight, and representing 90-95% of the total collagen content in the tissue. It forms fibrils that endow cartilage with tensile strength (Mayne, R. Arthritis Rhuem. 32:241-246 (1989)).

Summary

[0005] It has been discovered that certain polymorphic variations in human genomic DNA are associated with osteoarthritis. In particular, polymorphic variants in loci containing *PSMB1, TBP, PDCD2, ELP3, CHDC1* and *ERG* regions in human genomic DNA have been associated with risk of osteoarthritis. The *PSMB1, TBP* and *PDCD2* regions are located in a larger region referred to herein as the *chrom 6* region.

[0006] Thus, featured herein are methods for identifying a subject at risk of osteoarthritis and/or a risk of osteoarthritis in a subject, which comprise detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in or around the loci described herein in a human nucleic acid sample. In an embodiment, two or more polymorphic variations are detected in two or more regions, of which one or more is a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* region. In certain

embodiments, 3 or more, or 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 or more polymorphic variants are detected.

[0007] Also featured are nucleic acids that include one or more polymorphic variations associated with occurrence of osteoarthritis, as well as polypeptides encoded by these nucleic acids. In addition, provided are methods for identifying candidate therapeutic molecules for treating osteoarthritis, as well as methods for treating osteoarthritis in a subject by identifying a subject at risk of osteoarthritis and treating the subject with a suitable prophylactic, treatment or therapeutic molecule.

[0008] Also provided are compositions comprising a cell from a subject having osteoarthritis or at risk of osteoarthritis and/or a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid, with a RNAi, siRNA, antisense DNA or RNA, or ribozyme nucleic acid designed from a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence. In an embodiment, the RNAi, siRNA, antisense DNA or RNA, or ribozyme nucleic acid is designed from a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence that includes one or more polymorphic variations associated with osteoarthritis, and in some instances, specifically interacts with such a nucleotide sequence. Further, provided are arrays of nucleic acids bound to a solid surface, in which one or more nucleic acid molecules of the array have a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence, or a fragment or substantially identical nucleic acid thereof, or a complementary nucleic acid of the foregoing. Featured also are compositions comprising a cell from a subject having osteoarthritis or at risk of osteoarthritis and/or a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* polypeptide, with an antibody that specifically binds to the polypeptide. In an embodiment, the antibody specifically binds to an epitope in the polypeptide that includes a non-synonymous amino acid modification associated with osteoarthritis (e.g., results in an amino acid substitution in the encoded polypeptide associated with osteoarthritis). In certain embodiments, the antibody selectively binds to an epitope in the *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* polypeptide having an amino acid associated with osteoarthritis.

Brief Description of the Drawings

[0009] Figures 1A-1D show proximal SNPs in *chrom 6, ELP3, CHDC1* and *ERG* regions of genomic DNA, respectively. The position of each SNP in the chromosome is shown on the x-axis and the y-axis provides the negative logarithm of the p-value comparing the estimated allele to that of the control group. Also shown in the figures are exons and introns of the regions in the approximate chromosomal positions.

Detailed Description

[0010] It has been discovered that a polymorphic variant in a locus containing a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* region is associated with occurrence of osteoarthritis in subjects. Thus,

detecting genetic determinants associated with an increased risk of osteoarthritis occurrence can lead to early identification of a predisposition to osteoarthritis and early prescription of preventative measures. Also, associating a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* polymorphic variant with osteoarthritis has provided new targets for screening molecules useful in treatments of osteoarthritis.

Osteoarthritis and Sample Selection

[0011] Osteoarthritis (OA), or degenerative joint disease, is one of the oldest and most common types of arthritis. It is characterized by the breakdown of the joint's cartilage. Cartilage is the part of the joint that cushions the ends of bones, and its breakdown causes bones to rub against each other, causing pain and loss of movement. Type II collagen is the main component of cartilage, comprising 15-25% of the wet weight, approximately half the dry weight, and representing 90-95% of the total collagen content in the tissue. It forms fibrils that endow cartilage with tensile strength (Mayne, R. Arthritis Rhuem. 32:241-246 (1989)).

[0012] Most commonly affecting middle-aged and older people, OA can range from very mild to very severe. It affects hands and weight-bearing joints such as knees, hips, feet and the back. Knee OA can be as disabling as any cardiovascular disease except stroke.

[0013] Osteoarthritis affects an estimated 20.7 million Americans, mostly after age 45, with women more commonly affected than men. Physicians make a diagnosis of OA based on a physical exam and history of symptoms. X-rays are used to confirm diagnosis. Most people over 60 reflect the disease on X-ray, and about one-third have actual symptoms.

[0014] There are many factors that can cause OA. Obesity may lead to osteoarthritis of the knees. In addition, people with joint injuries due to sports, work-related activity or accidents may be at increased risk of developing OA.

[0015] Genetics has a role in the development of OA. Some people may be born with defective cartilage or with slight defects in the way that joints fit together. As a person ages, these defects may cause early cartilage breakdown in the joint or the inability to repair damaged or deteriorated cartilage in the joint.

[0016] Inclusion or exclusion of samples for an osteoarthritis pool may be based upon the following criteria: ethnicity (e.g., samples derived from an individual characterized as Caucasian); parental ethnicity (e.g., samples derived from an individual of British paternal and maternal descent); relevant phenotype information for the individual (e.g., case samples derived from individuals diagnosed with specific knee osteoarthritis (OA) and were recruited from an OA knee replacement clinic). Control samples may be selected based on relevant phenotype information for the individual (e.g., derived from individuals free of OA at several sites (knee, hand, hip etc)); and no family history of OA and/or rheumatoid arthritis. Additional phenotype information collected for both cases and controls may include

age of the individual, gender, family history of OA, diagnosis with osteoarthritis (joint location of OA, date of primary diagnosis, age of individual as of primary diagnosis), knee history (current symptoms, any major knee injury, menisectomy, knee replacement surgery, age of surgery), HRT history, osteoporosis diagnosis.

[0017] Based in part upon selection criteria set forth above, individuals having osteoarthritis can be selected for genetic studies. Also, individuals having no history of osteoarthritis often are selected for genetic studies, as described hereafter.

Polymorphic Variants Associated with Osteoarthritis

[0018] A genetic analysis provided herein linked osteoarthritis with polymorphic variant nucleic acid sequences in the human genome. As used herein, the term "polymorphic site" refers to a region in a nucleic acid at which two or more alternative nucleotide sequences are observed in a significant number of nucleic acid samples from a population of individuals. A polymorphic site may be a nucleotide sequence of two or more nucleotides, an inserted nucleotide or nucleotide sequence, a deleted nucleotide or nucleotide sequence, or a microsatellite, for example. A polymorphic site that is two or more nucleotides in length may be 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more, 20 or more, 30 or more, 50 or more, 75 or more, 100 or more, 500 or more, or about 1000 nucleotides in length, where all or some of the nucleotide sequences differ within the region. A polymorphic site is often one nucleotide in length, which is referred to herein as a "single nucleotide polymorphism" or a "SNP."

[0019] Where there are two, three, or four alternative nucleotide sequences at a polymorphic site, each nucleotide sequence is referred to as a "polymorphic variant" or "nucleic acid variant." Where two polymorphic variants exist, for example, the polymorphic variant represented in a minority of samples from a population is sometimes referred to as a "minor allele" and the polymorphic variant that is more prevalently represented is sometimes referred to as a "major allele." Many organisms possess a copy of each chromosome (*e.g.*, humans), and those individuals who possess two major alleles or two minor alleles are often referred to as being "homozygous" with respect to the polymorphism, and those individuals who possess one major allele and one minor allele are normally referred to as being "heterozygous" with respect to the polymorphism. Individuals who are homozygous with respect to one allele are sometimes predisposed to a different phenotype as compared to individuals who are heterozygous or homozygous with respect to another allele.

[0020] In genetic analysis that associate polymorphic variants with osteoarthritis, samples from individuals having osteoarthritis and individuals not having osteoarthritis often are allelotyped and/or genotyped. The term "allelotype" as used herein refers to a process for determining the allele frequency for a polymorphic variant in pooled DNA samples from cases and controls. By pooling DNA from each group, an allele frequency for each SNP in each group is calculated. These allele frequencies are then

compared to one another. The term "genotyped" as used herein refers to a process for determining a genotype of one or more individuals, where a "genotype" is a representation of one or more polymorphic variants in a population.

[0021] A genotype or polymorphic variant may be expressed in terms of a "haplotype," which as used herein refers to two or more polymorphic variants occurring within genomic DNA in a group of individuals within a population. For example, two SNPs may exist within a gene where each SNP position includes a cytosine variation and an adenine variation. Certain individuals in a population may carry one allele (heterozygous) or two alleles (homozygous) having the gene with a cytosine at each SNP position. As the two cytosines corresponding to each SNP in the gene travel together on one or both alleles in these individuals, the individuals can be characterized as having a cytosine/cytosine haplotype with respect to the two SNPs in the gene.

[0022] As used herein, the term "phenotype" refers to a trait which can be compared between individuals, such as presence or absence of a condition, a visually observable difference in appearance between individuals, metabolic variations, physiological variations, variations in the function of biological molecules, and the like. An example of a phenotype is occurrence of osteoarthritis.

[0023] Researchers sometimes report a polymorphic variant in a database without determining whether the variant is represented in a significant fraction of a population. Because a subset of these reported polymorphic variants are not represented in a statistically significant portion of the population, some of them are sequencing errors and/or not biologically relevant. Thus, it is often not known whether a reported polymorphic variant is statistically significant or biologically relevant until the presence of the variant is detected in a population of individuals and the frequency of the variant is determined. Methods for detecting a polymorphic variant in a population are described herein, specifically in Example 2. A polymorphic variant is statistically significant and often biologically relevant if it is represented in 5% or more of a population, sometimes 10% or more, 15% or more, or 20% or more of a population, and often 25% or more, 30% or more, 35% or more, 40% or more, 45% or more, or 50% or more of a population.

[0024] A polymorphic variant may be detected on either or both strands of a double-stranded nucleic acid. Also, a polymorphic variant may be located within an intron or exon of a gene or within a portion of a regulatory region such as a promoter, a 5′ untranslated region (UTR), a 3′ UTR, and in DNA (*e.g.*, genomic DNA (gDNA) and complementary DNA (cDNA)), RNA (*e.g.*, mRNA, tRNA, and rRNA), or a polypeptide. Polymorphic variations may or may not result in detectable differences in gene expression, polypeptide structure, or polypeptide function.

[0025] It was determined that polymorphic variations associated with an increased risk of osteoarthritis existed in the *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* regions. In certain embodiments, polymorphic variants at positions rs756519, rs1042327, rs8770, rs1563055, rs912428 and rs1888475 in the human genome were associated with an increased risk of osteoarthritis, and in specific

embodiments, a thymine at position rs756519, a cytosine at position rs1042327, a cytosine at position rs8770, a thymine at position rs1563055, a thymine at position rs912428 and an adenine at position rs1888475 were associated with an increased risk of osteoarthritis.

[0026] Polymorphic variants in and around the *chrom 6* region were tested for association with osteoarthritis. These include polymorphic variants at positions in SEQ ID NO: 1 selected from the group consisting of 229, 6310, 11840, 11870, 12064, 13392, 16354, 16559, 16935, 17616, 17737, 18321, 18453, 18811, 20020, 21662, 23197, 23446, 24339, 25504, 27174, 28008, 29294, 29759, 30832, 44512, 44850, 45884, 46345, 48589, 53371, 53911, 53990, 55152, 55667, 58952, 59315, 60029, 61477, 62988, 63090, 64021, 65685, 70220, 70323, 70959, 73436, 82945, 82958, 82961, 82964, 82965, 83006, 83025, 83034, 83074 ,83132, 83155, 83172, 83174, 83206, 83216, 83234, 83252, 83260, 83263, 83296, 83319, 83322, 83324, 83357, 83375, 83381, 83389, 83443, 83499, 83545, 83566, 83591, 83619, 83698, 83780, 83784, 83826, 83832, 83852, 86297, 86315, 86420, 86460, 86714, 86718, 86736, 86753, 86766, 88162, 88218, 88246, 88255, 88309, 88310, 88471, 88619, 88904, 89044, 90531, 90534, 90613 and 46252. Polymorphic variants at the following positions in SEQ ID NO: 1 in particular were associated with an increased risk of osteoarthritis: 229, 6310, 16559, 18453, 25504, 27174, 30832, 44850, 45884, 48589, 61477, 82961 and 46252, with specific embodiments directed to variants at positions 229, 16559, 44850 and/or 46252. In particular, the following polymorphic variants in SEQ ID NO: 1 were associated with risk of osteoarthritis: a thymine at position 229, a guanine at position 6310, a thymine at position 16559, an adenine at position 18453, an adenine at position 25504, an adenine at position 27174, an adenine at position 30832, a guanine at position 44850, an adenine at position 45884, an adenine at position 48589, a cytosine at position 61477, a cytosine at position 82961 and a thymine at position 46252.

[0027] Polymorphic variants in and around the *ELP3* region were tested for association with osteoarthritis. These include polymorphic variants at positions in SEQ ID NO: 2 selected from the group consisting of 211, 473, 1536, 5639, 17186, 17335, 25029, 25111, 28811, 28863, 30809, 40985, 45147, 45282, 46168, 46328, 49077, 51925, 52141, 52168, 60852, 62468, 65572, 79089, 79541, 79790, 90843, 90978, 91052, 91131, 91132, 94439 and 94621. Polymorphic variants at the following positions in SEQ ID NO: 2 in particular were associated with an increased risk of osteoarthritis: 40985, 46168, 51925 and 52168. In particular, the following polymorphic variants in SEQ ID NO: 2 were associated with risk of osteoarthritis: a cytosine at position 40985, a guanine at position 46168, a thymine at position 51925 and a cytosine at position 52168.

[0028] Polymorphic variants in and around the *CHDC1* region were tested for association with osteoarthritis. These include polymorphic variants at positions in SEQ ID NO: 3 selected from the group consisting of 243, 10208, 15049, 15111, 15272, 15287, 15326, 15327, 17038, 19391, 21702, 22431, 22881, 27744, 32564, 32698, 33104, 33181, 33256, 33543, 35567, 40085, 40482, 45641, 46059, 48504, 48919, 49693, 49874, 50020, 50616, 50719, 55511, 65533, 70529, 75591, 77266, 80368, 82475, 92462,

92480, 95819 and 96275. Polymorphic variants at the following positions in SEQ ID NO: 3 in particular were associated with an increased risk of osteoarthritis: 15111, 45641, 46059, 49693, 49874, 50020, 50719, 70529, 82475, 92462, 92480 and 96275, with specific embodiments directed to variants at positions 82475 and/or 92462. In particular, the following polymorphic variants in SEQ ID NO: 3 were associated with risk of osteoarthritis: a guanine at position 15111, a thymine at position 45641, an adenine at position 46059, a cytosine at position 49693, an adenine at position 49874, an adenine at position 50020, a guanine at position 50719, an adenine at position 70529, an adenine at position 82475, a thymine at position 92462, a thymine at position 92480 and a cytosine at position 96275.

[0029] Polymorphic variants in and around the *ERG* region were tested for association with osteoarthritis. These include polymorphic variants at positions in SEQ ID NO: 4 selected from the group consisting of 231, 882, 960, 1194, 1530, 1673, 2096, 2285, 5873, 7256, 7988, 8222, 8381, 8814, 8915, 9642, 9902, 10619, 10927, 11032, 14377, 15608, 15928, 16296, 17598, 19272, 20084, 20577, 28051, 29466, 29530, 29987, 30012, 30322, 32216, 32516, 32544, 32746, 33137, 33538, 33798, 33802, 33964, 34132, 34210, 34317, 34499, 34753, 34845, 35335, 36423, 36450, 36481, 38447, 38784, 39387, 39458, 39822, 40305, 40869, 40926, 41010, 41134, 41984, 42172, 42753, 43011, 43176, 43320, 43381, 44142, 44383, 44726, 45087, 45141, 45359, 45421, 45456, 45467, 45486, 45709, 45716, 47626, 49413, 49796, 49962, 50075, 50093, 50571, 50615, 50780, 50851, 51459, 53193, 53702, 53736, 53795, 54109, 54126, 54230, 54894, 55455, 55499, 56522, 56662, 56954, 57267, 58282, 58916, 59544, 59666, 59913, 66846, 67245, 67652, 67955, 67966, 68420, 70226, 70810, 72246, 73330, 73457, 74389, 74638, 74640, 75358, 75952, 76098, 77836, 78449, 78507, 80031, 81695, 82775, 82795, 84611, 84657, 84693, 85020, 85048, 85100, 85325, 85452, 85868, 85936, 85990, 86139, 86497, 87236, 87248, 87533, 87912, 88108, 88494, 89598, 90235, 91287, 91359, 92384, 92410, 92900, 94495, 94512, 97777 and 98333. Polymorphic variants at the following positions in SEQ ID NO: 4 in particular were associated with an increased risk of osteoarthritis: 1673, 20577, 33137, 39822, 45716, 49962, 51459, 54894, 55455, 55499, 58282, 68420 and 80031, with specific embodiments directed to variants at positions 33137, 55499 and/or 58282. In particular, the following polymorphic variants in SEQ ID NO: 4 were associated with risk of osteoarthritis: a guanine at position 1673, a thymine at position 20577, a guanine at position 33137, a guanine at position 39822, an adenine at position 45716, a guanine at position 49962, an adenine at position 51459, a cytosine at position 54894, an adenine at position 55455, an adenine at position 55499, a guanine at position 58282, an adenine at position 68420 and a thymine at position 80031.

[0030] Based in part upon analyses summarized in Figures 1A-1D, regions with significant association have been identified in loci associated with osteoarthritis. Any polymorphic variants associated with osteoarthritis in a region of significant association can be utilized for embodiments described herein. For example, polymorphic variants in a region spanning chromosome positions 170719500 to 170766500 (approximately 47,000 nucleotides in length) in a *chrom 6* region, spanning

chromosome positions 27963000 to 27983000 (approximately 20,000 nucleotides in length) in a *ELP3* region, spanning chromosome positions 44962000 to 45013000 (approximately 51,000 nucleotides in length) in a *CHDC1* region, and spanning chromosome positions 38830000 to 38844000 (approximately 14,000 nucleotides in length) in a *ERG* region, have significant association (chromosome positions are within NCBI's Genome build 34).

Additional Polymorphic Variants Associated with Osteoarthritis

[0031] Also provided is a method for identifying polymorphic variants proximal to an incident, founder polymorphic variant associated with osteoarthritis. Thus, featured herein are methods for identifying a polymorphic variation associated with osteoarthritis that is proximal to an incident polymorphic variation associated with osteoarthritis, which comprises identifying a polymorphic variant proximal to the incident polymorphic variant associated with osteoarthritis, where the incident polymorphic variant is in a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence. The nucleotide sequence often comprises a polynucleotide sequence selected from the group consisting of (a) a polynucleotide sequence of SEQ ID NO: 1-12; (b) a polynucleotide sequence that encodes a polypeptide having an amino acid sequence encoded by a polynucleotide sequence of SEQ ID NO: 1-12; and (c) a polynucleotide sequence that encodes a polypeptide having an amino acid sequence that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1 or a polynucleotide sequence 90% or more identical to the polynucleotide sequence of SEQ ID NO: 1-12. The presence or absence of an association of the proximal polymorphic variant with osteoarthritis then is determined using a known association method, such as a method described in the Examples hereafter. In an embodiment, the incident polymorphic variant is a polymorphic variant associated with osteoarthritis described herein. In another embodiment, the proximal polymorphic variant identified sometimes is a publicly disclosed polymorphic variant, which for example, sometimes is published in a publicly available database. In other embodiments, the polymorphic variant identified is not publicly disclosed and is discovered using a known method, including, but not limited to, sequencing a region surrounding the incident polymorphic variant in a group of nucleic samples. Thus, multiple polymorphic variants proximal to an incident polymorphic variant are associated with osteoarthritis using this method.

[0032] The proximal polymorphic variant often is identified in a region surrounding the incident polymorphic variant. In certain embodiments, this surrounding region is about 50 kb flanking the first polymorphic variant (*e.g.* about 50 kb 5' of the first polymorphic variant and about 50 kb 3' of the first polymorphic variant), and the region sometimes is composed of shorter flanking sequences, such as flanking sequences of about 40 kb, about 30 kb, about 25 kb, about 20 kb, about 15 kb, about 10 kb, about 7 kb, about 5 kb, or about 2 kb 5' and 3' of the incident polymorphic variant. In other embodiments, the region is composed of longer flanking sequences, such as flanking sequences of about

55 kb, about 60 kb, about 65 kb, about 70 kb, about 75 kb, about 80 kb, about 85 kb, about 90 kb, about 95 kb, or about 100 kb 5' and 3' of the incident polymorphic variant.

[0033] In certain embodiments, polymorphic variants associated with osteoarthritis are identified iteratively. For example, a first proximal polymorphic variant is associated with osteoarthritis using the methods described above and then another polymorphic variant proximal to the first proximal polymorphic variant is identified (*e.g.*, publicly disclosed or discovered) and the presence or absence of an association of one or more other polymorphic variants proximal to the first proximal polymorphic variant with osteoarthritis is determined.

[0034] The methods described herein are useful for identifying or discovering additional polymorphic variants that may be used to further characterize a gene, region or loci associated with a condition, a disease (*e.g.*, osteoarthritis), or a disorder. For example, allelotyping or genotyping data from the additional polymorphic variants may be used to identify a functional mutation or a region of linkage disequilibrium. In certain embodiments, polymorphic variants identified or discovered within a region comprising the first polymorphic variant associated with osteoarthritis are genotyped using the genetic methods and sample selection techniques described herein, and it can be determined whether those polymorphic variants are in linkage disequilibrium with the first polymorphic variant. The size of the region in linkage disequilibrium with the first polymorphic variant also can be assessed using these genotyping methods. Thus, provided herein are methods for determining whether a polymorphic variant is in linkage disequilibrium with a first polymorphic variant associated with osteoarthritis, and such information can be used in prognosis/diagnosis methods described herein.

Isolated Nucleic Acids

[0035] Featured herein are isolated *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid variants depicted in SEQ ID NO: 1-12, and substantially identical nucleic acids thereof. A nucleic acid variant may be represented on one or both strands in a double-stranded nucleic acid or on one chromosomal complement (heterozygous) or both chromosomal complements (homozygous).

[0036] As used herein, the term "nucleic acid" includes DNA molecules (*e.g.*, a complementary DNA (cDNA) and genomic DNA (gDNA)) and RNA molecules (*e.g.*, mRNA, rRNA, siRNA and tRNA) and analogs of DNA or RNA, for example, by use of nucleotide analogs. The nucleic acid molecule can be single-stranded and it is often double-stranded. The term "isolated or purified nucleic acid" refers to nucleic acids that are separated from other nucleic acids present in the natural source of the nucleic acid. For example, with regard to genomic DNA, the term "isolated" includes nucleic acids which are separated from the chromosome with which the genomic DNA is naturally associated. An "isolated" nucleic acid is often free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5' and/or 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic

acid is derived. For example, in various embodiments, the isolated nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of 5' and/or 3' nucleotide sequences which flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. As used herein, the term "gene" refers to a nucleotide sequence that encodes a polypeptide.

[0037] Also included herein are nucleic acid fragments. These fragments often have a nucleotide sequence identical to a nucleotide sequence of SEQ ID NO: 1-12, a nucleotide sequence substantially identical to a nucleotide sequence of SEQ ID NO: 1-12, or a nucleotide sequence that is complementary to the foregoing. The nucleic acid fragment may be identical, substantially identical or homologous to a nucleotide sequence in an exon or an intron in a nucleotide sequence of SEQ ID NO: 1-12, and may encode a domain or part of a domain of a polypeptide. Sometimes, the fragment will comprises one or more of the polymorphic variations described herein as being associated with osteoarthritis. The nucleic acid fragment is often 50, 100, or 200 or fewer base pairs in length, and is sometimes about 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, 1500, 2000, 3000, 4000, 5000, 10000, 15000, or 20000 base pairs in length. A nucleic acid fragment that is complementary to a nucleotide sequence identical or substantially identical to a nucleotide sequence in SEQ ID NO: 1-12 and hybridizes to such a nucleotide sequence under stringent conditions is often referred to as a "probe." Nucleic acid fragments often include one or more polymorphic sites, or sometimes have an end that is adjacent to a polymorphic site as described hereafter.

[0038] An example of a nucleic acid fragment is an oligonucleotide. As used herein, the term "oligonucleotide" refers to a nucleic acid comprising about 8 to about 50 covalently linked nucleotides, often comprising from about 8 to about 35 nucleotides, and more often from about 10 to about 25 nucleotides. The backbone and nucleotides within an oligonucleotide may be the same as those of naturally occurring nucleic acids, or analogs or derivatives of naturally occurring nucleic acids, provided that oligonucleotides having such analogs or derivatives retain the ability to hybridize specifically to a nucleic acid comprising a targeted polymorphism. Oligonucleotides described herein may be used as hybridization probes or as components of prognostic or diagnostic assays, for example, as described herein.

[0039] Oligonucleotides are typically synthesized using standard methods and equipment, such as the ABI™3900 High Throughput DNA Synthesizer and the EXPEDITE™ 8909 Nucleic Acid Synthesizer, both of which are available from Applied Biosystems (Foster City, CA). Analogs and derivatives are exemplified in U.S. Pat. Nos. 4,469,863; 5,536,821; 5,541,306; 5,637,683; 5,637,684;

5,700,922; 5,717,083; 5,719,262; 5,739,308; 5,773,601; 5,886,165; 5,929,226; 5,977,296; 6,140,482; WO 00/56746; WO 01/14398, and related publications. Methods for synthesizing oligonucleotides comprising such analogs or derivatives are disclosed, for example, in the patent publications cited above and in U.S. Pat. Nos. 5,614,622; 5,739,314; 5,955,599; 5,962,674; 6,117,992; in WO 00/75372; and in related publications.

[0040] Oligonucleotides may also be linked to a second moiety. The second moiety may be an additional nucleotide sequence such as a tail sequence (*e.g.*, a polyadenosine tail), an adapter sequence (*e.g.*, phage M13 universal tail sequence), and others. Alternatively, the second moiety may be a non-nucleotide moiety such as a moiety which facilitates linkage to a solid support or a label to facilitate detection of the oligonucleotide. Such labels include, without limitation, a radioactive label, a fluorescent label, a chemiluminescent label, a paramagnetic label, and the like. The second moiety may be attached to any position of the oligonucleotide, provided the oligonucleotide can hybridize to the nucleic acid comprising the polymorphism.

Uses for Nucleic Acid Sequence

[0041] Nucleic acid coding sequences may be used for diagnostic purposes for detection and control of polypeptide expression. Also, included herein are oligonucleotide sequences such as antisense RNA, small-interfering RNA (siRNA) and DNA molecules and ribozymes that function to inhibit translation of a polypeptide. Antisense techniques and RNA interference techniques are known in the art and are described herein.

[0042] Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. The mechanism of ribozyme action involves sequence specific hybridization of the ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. For example, hammerhead motif ribozyme molecules may be engineered that specifically and efficiently catalyze endonucleolytic cleavage of RNA sequences corresponding to or complementary to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence. Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites which include the following sequences, GUA, GUU and GUC. Once identified, short RNA sequences of between fifteen (15) and twenty (20) ribonucleotides corresponding to the region of the target gene containing the cleavage site may be evaluated for predicted structural features such as secondary structure that may render the oligonucleotide sequence unsuitable. The suitability of candidate targets may also be evaluated by testing their accessibility to hybridization with complementary oligonucleotides, using ribonuclease protection assays.

[0043] Antisense RNA and DNA molecules, siRNA and ribozymes may be prepared by any method known in the art for the synthesis of RNA molecules. These include techniques for chemically

synthesizing oligodeoxyribonucleotides well known in the art such as solid phase phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by *in vitro* and *in vivo* transcription of DNA sequences encoding the antisense RNA molecule. Such DNA sequences may be incorporated into a wide variety of vectors which incorporate suitable RNA polymerase promoters such as the T7 or SP6 polymerase promoters. Alternatively, antisense cDNA constructs that synthesize antisense RNA constitutively or inducibly, depending on the promoter used, can be introduced stably into cell lines.

[0044] DNA encoding a polypeptide also may have a number of uses for the diagnosis of diseases, including osteoarthritis, resulting from aberrant expression of a target gene described herein. For example, the nucleic acid sequence may be used in hybridization assays of biopsies or autopsies to diagnose abnormalities of expression or function (*e.g.*, Southern or Northern blot analysis, in situ hybridization assays).

[0045] In addition, the expression of a polypeptide during embryonic development may also be determined using nucleic acid encoding the polypeptide. As addressed, *infra*, production of functionally impaired polypeptide is the cause of various disease states, such as osteoarthritis. *In situ* hybridizations using polypeptide as a probe may be employed to predict problems related to osteoarthritis. Further, as indicated, *infra*, administration of human active polypeptide, recombinantly produced as described herein, may be used to treat disease states related to functionally impaired polypeptide. Alternatively, gene therapy approaches may be employed to remedy deficiencies of functional polypeptide or to replace or compete with dysfunctional polypeptide.

Expression Vectors, Host Cells, and Genetically Engineered Cells

[0046] Provided herein are nucleic acid vectors, often expression vectors, which contain a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence, or a substantially identical sequence thereof. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked and can include a plasmid, cosmid, or viral vector. The vector can be capable of autonomous replication or it can integrate into a host DNA. Viral vectors may include replication defective retroviruses, adenoviruses and adeno-associated viruses for example.

[0047] A vector can include a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence in a form suitable for expression of an encoded target polypeptide or target nucleic acid in a host cell. A "target polypeptide" is a polypeptide encoded by a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence, or a substantially identical nucleotide sequence thereof. The recombinant expression vector typically includes one or more regulatory sequences operatively linked to the nucleic acid sequence to be expressed. The term "regulatory sequence" includes promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Regulatory sequences include those that direct constitutive expression of a nucleotide sequence, as well as tissue-specific regulatory and/or

inducible sequences. The design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of polypeptide desired, and the like. Expression vectors can be introduced into host cells to produce target polypeptides, including fusion polypeptides.

[0048] Recombinant expression vectors can be designed for expression of target polypeptides in prokaryotic or eukaryotic cells. For example, target polypeptides can be expressed in *E. coli*, insect cells (*e.g.*, using baculovirus expression vectors), yeast cells, or mammalian cells. Suitable host cells are discussed further in Goeddel, *Gene Expression Technology: Methods in Enzymology 185*, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

[0049] Expression of polypeptides in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion polypeptides. Fusion vectors add a number of amino acids to a polypeptide encoded therein, usually to the amino terminus of the recombinant polypeptide. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant polypeptide; 2) to increase the solubility of the recombinant polypeptide; and 3) to aid in the purification of the recombinant polypeptide by acting as a ligand in affinity purification. Often, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant polypeptide to enable separation of the recombinant polypeptide from the fusion moiety subsequent to purification of the fusion polypeptide. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith & Johnson, *Gene 67:* 31-40 (1988)), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding polypeptide, or polypeptide A, respectively, to the target recombinant polypeptide.

[0050] Purified fusion polypeptides can be used in screening assays and to generate antibodies specific for target polypeptides. In a therapeutic embodiment, fusion polypeptide expressed in a retroviral expression vector is used to infect bone marrow cells that are subsequently transplanted into irradiated recipients. The pathology of the subject recipient is then examined after sufficient time has passed (*e.g.*, six (6) weeks).

[0051] Expressing the polypeptide in host bacteria with an impaired capacity to proteolytically cleave the recombinant polypeptide is often used to maximize recombinant polypeptide expression (Gottesman, S., *Gene Expression Technology: Methods in Enzymology, Academic Press, San Diego, California 185:* 119-128 (1990)). Another strategy is to alter the nucleotide sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada *et al., Nucleic Acids Res. 20:* 2111-2118 (1992)). Such alteration of nucleotide sequences can be carried out by standard DNA synthesis techniques.

[0052] When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. Recombinant mammalian expression vectors are often capable of directing expression of the nucleic acid in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Non-limiting examples of suitable tissue-specific promoters include an albumin promoter (liver-specific; Pinkert *et al., Genes Dev. 1:* 268-277 (1987)), lymphoid-specific promoters (Calame & Eaton, *Adv. Immunol. 43:* 235-275 (1988)), promoters of T cell receptors (Winoto & Baltimore, *EMBO J. 8:* 729-733 (1989)) promoters of immunoglobulins (Banerji *et al., Cell 33:* 729-740 (1983); Queen & Baltimore, *Cell 33:* 741-748 (1983)), neuron-specific promoters (*e.g.*, the neurofilament promoter; Byrne & Ruddle, *Proc. Natl. Acad. Sci. USA 86:* 5473-5477 (1989)), pancreas-specific promoters (Edlund *et al., Science 230:* 912-916 (1985)), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are sometimes utilized, for example, the murine hox promoters (Kessel & Gruss, *Science 249:* 374-379 (1990)) and the α-fetopolypeptide promoter (Campes & Tilghman, *Genes Dev. 3:* 537-546 (1989)).

[0053] A *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid also may be cloned into an expression vector in an antisense orientation. Regulatory sequences (*e.g.*, viral promoters and/or enhancers) operatively linked to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid cloned in the antisense orientation can be chosen for directing constitutive, tissue specific or cell type specific expression of antisense RNA in a variety of cell types. Antisense expression vectors can be in the form of a recombinant plasmid, phagemid or attenuated virus. For a discussion of the regulation of gene expression using antisense genes *see, e.g.*, Weintraub *et al.*, Antisense RNA as a molecular tool for genetic analysis, *Reviews - Trends in Genetics*, Vol. 1(1) (1986).

[0054] Also provided herein are host cells that include a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence within a recombinant expression vector or a fragment of such a nucleotide sequence which facilitate homologous recombination into a specific site of the host cell genome. The terms "host cell" and "recombinant host cell" are used interchangeably herein. Such terms refer not only to the particular subject cell but rather also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein. A host cell can be any prokaryotic or eukaryotic cell. For example, a target polypeptide can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

[0055] Vectors can be introduced into host cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.*, DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, transduction/infection, DEAE-dextran-mediated transfection, lipofection, or electroporation.

[0056] A host cell provided herein can be used to produce (*i.e.*, express) a target polypeptide or a substantially identical polypeptide thereof. Accordingly, further provided are methods for producing a target polypeptide using host cells described herein. In one embodiment, the method includes culturing host cells into which a recombinant expression vector encoding a target polypeptide has been introduced in a suitable medium such that a target polypeptide is produced. In another embodiment, the method further includes isolating a target polypeptide from the medium or the host cell.

[0057] Also provided are cells or purified preparations of cells which include a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* transgene, or which otherwise misexpress target polypeptide. Cell preparations can consist of human or non-human cells, *e.g.*, rodent cells, *e.g.*, mouse or rat cells, rabbit cells, or pig cells. In preferred embodiments, the cell or cells include a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* transgene (*e.g.*, a heterologous form of a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* gene, such as a human gene expressed in non-human cells). The transgene can be misexpressed, *e.g.*, overexpressed or underexpressed. In other preferred embodiments, the cell or cells include a gene which misexpress an endogenous target polypeptide (*e.g.*, expression of a gene is disrupted, also known as a knockout). Such cells can serve as a model for studying disorders which are related to mutated or mis-expressed alleles or for use in drug screening. Also provided are human cells (*e.g.*, a hematopoietic stem cells) transfected with a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid.

[0058] Also provided are cells or a purified preparation thereof (*e.g.*, human cells) in which an endogenous *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid is under the control of a regulatory sequence that does not normally control the expression of the endogenous gene. The expression characteristics of an endogenous gene within a cell (*e.g.*, a cell line or microorganism) can be modified by inserting a heterologous DNA regulatory element into the genome of the cell such that the inserted regulatory element is operably linked to the corresponding endogenous gene. For example, an endogenous corresponding gene (*e.g.*, a gene which is "transcriptionally silent," not normally expressed, or expressed only at very low levels) may be activated by inserting a regulatory element which is capable of promoting the expression of a normally expressed gene product in that cell. Techniques such as targeted homologous recombinations, can be used to insert the heterologous DNA as described in, *e.g.*, Chappel, US 5,272,071; WO 91/06667, published on May 16, 1991.

Transgenic Animals

[0059] Non-human transgenic animals that express a heterologous target polypeptide (*e.g.*, expressed from a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid or substantially identical sequence thereof) can be generated. Such animals are useful for studying the function and/or activity of a target polypeptide and for identifying and/or evaluating modulators of the activity of a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid or encoded polypeptide. As used herein, a "transgenic animal" is a non-human animal such as a mammal (*e.g.*, a non-human primate such as chimpanzee, baboon, or macaque; an ungulate such as an equine, bovine, or caprine; or a rodent such as a rat, a mouse, or an Israeli sand rat), a bird (*e.g.*, a chicken or a turkey), an amphibian (*e.g.*, a frog, salamander, or newt), or an insect (*e.g.*, *Drosophila melanogaster*), in which one or more of the cells of the animal includes a transgene. A transgene is exogenous DNA or a rearrangement (*e.g.*, a deletion of endogenous chromosomal DNA) that is often integrated into or occurs in the genome of cells in a transgenic animal. A transgene can direct expression of an encoded gene product in one or more cell types or tissues of the transgenic animal, and other transgenes can reduce expression (*e.g.*, a knockout). Thus, a transgenic animal can be one in which an endogenous nucleic acid homologous to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal (*e.g.*, an embryonic cell of the animal) prior to development of the animal.

[0060] Intronic sequences and polyadenylation signals can also be included in the transgene to increase expression efficiency of the transgene. One or more tissue-specific regulatory sequences can be operably linked to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence to direct expression of an encoded polypeptide to particular cells. A transgenic founder animal can be identified based upon the presence of a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence in its genome and/or expression of encoded mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence can further be bred to other transgenic animals carrying other transgenes.

[0061] Target polypeptides can be expressed in transgenic animals or plants by introducing, for example, a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid into the genome of an animal that encodes the target polypeptide. In preferred embodiments the nucleic acid is placed under the control of a tissue specific promoter, *e.g.*, a milk or egg specific promoter, and recovered from the milk or eggs produced by the animal. Also included is a population of cells from a transgenic animal.

Target Polypeptides

[0062] Also featured herein are isolated target polypeptides, which are encoded by a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence (e.g., SEQ ID NO: 1-12), or a substantially identical nucleotide sequence thereof. Examples of *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* polypeptides are set forth in SEQ ID NO: 13-20. The term "polypeptide" as used herein includes proteins and peptides. An "isolated" or "purified" polypeptide or protein is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. In one embodiment, the language "substantially free" means preparation of a target polypeptide having less than about 30%, 20%, 10% and more preferably 5% (by dry weight), of non-target polypeptide (also referred to herein as a "contaminating protein"), or of chemical precursors or non-target chemicals. When the target polypeptide or a biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, specifically, where culture medium represents less than about 20%, sometimes less than about 10%, and often less than about 5% of the volume of the polypeptide preparation. Isolated or purified target polypeptide preparations are sometimes 0.01 milligrams or more or 0.1 milligrams or more, and often 1.0 milligrams or more and 10 milligrams or more in dry weight.

[0063] Further included herein are target polypeptide fragments. The polypeptide fragment may be a domain or part of a domain of a target polypeptide. The polypeptide fragment may have increased, decreased or unexpected biological activity. The polypeptide fragment is often 50 or fewer, 100 or fewer, or 200 or fewer amino acids in length, and is sometimes 300, 400, 500, 600, 700, or 900 or fewer amino acids in length. Certain embodiments are directed to *PSMB1* polypeptide fragments (e.g., sequence accessed by NP_002784; rs756519 in Table A), such as a proteasome protease domain (e.g., starting at about amino acid 34 and ending at about amino acid 226) or a proteasome B domain (e.g., starting at about amino acid 41 and ending at about amino acid 88).

[0064] Substantially identical target polypeptides may depart from the amino acid sequences of target polypeptides in different manners. For example, conservative amino acid modifications may be introduced at one or more positions in the amino acid sequences of target polypeptides. A "conservative amino acid substitution" is one in which the amino acid is replaced by another amino acid having a similar structure and/or chemical function. Families of amino acid residues having similar structures and functions are well known. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine,

tryptophan, histidine). Also, essential and non-essential amino acids may be replaced. A "non-essential" amino acid is one that can be altered without abolishing or substantially altering the biological function of a target polypeptide, whereas altering an "essential" amino acid abolishes or substantially alters the biological function of a target polypeptide. Amino acids that are conserved among target polypeptides are typically essential amino acids. In certain embodiments, the polypeptide includes one or more non-synonymous polymorphic variants associated with osteoarthritis.

[0065] Also, target polypeptides may exist as chimeric or fusion polypeptides. As used herein, a target "chimeric polypeptide" or target "fusion polypeptide" includes a target polypeptide linked to a non-target polypeptide. A "non-target polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a polypeptide which is not substantially identical to the target polypeptide, which includes, for example, a polypeptide that is different from the target polypeptide and derived from the same or a different organism. The target polypeptide in the fusion polypeptide can correspond to an entire or nearly entire target polypeptide or a fragment thereof. The non-target polypeptide can be fused to the N-terminus or C-terminus of the target polypeptide.

[0066] Fusion polypeptides can include a moiety having high affinity for a ligand. For example, the fusion polypeptide can be a GST-target fusion polypeptide in which the target sequences are fused to the C-terminus of the GST sequences, or a polyhistidine-target fusion polypeptide in which the target polypeptide is fused at the N- or C-terminus to a string of histidine residues. Such fusion polypeptides can facilitate purification of recombinant target polypeptide. Expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide), and a nucleotide sequence in SEQ ID NO: 1-12, or a substantially identical nucleotide sequence thereof, can be cloned into an expression vector such that the fusion moiety is linked in-frame to the target polypeptide. Further, the fusion polypeptide can be a target polypeptide containing a heterologous signal sequence at its N-terminus. In certain host cells (*e.g.*, mammalian host cells), expression, secretion, cellular internalization, and cellular localization of a target polypeptide can be increased through use of a heterologous signal sequence. Fusion polypeptides can also include all or a part of a serum polypeptide (*e.g.*, an IgG constant region or human serum albumin).

[0067] Target polypeptides can be incorporated into pharmaceutical compositions and administered to a subject *in vivo*. Administration of these target polypeptides can be used to affect the bioavailability of a substrate of the target polypeptide and may effectively increase target polypeptide biological activity in a cell. Target fusion polypeptides may be useful therapeutically for the treatment of disorders caused by, for example, (i) aberrant modification or mutation of a gene encoding a target polypeptide; (ii) mis-regulation of the gene encoding the target polypeptide; and (iii) aberrant post-translational modification of a target polypeptide. Also, target polypeptides can be used as immunogens to produce anti-target

antibodies in a subject, to purify target polypeptide ligands or binding partners, and in screening assays to identify molecules which inhibit or enhance the interaction of a target polypeptide with a substrate.

[0068] In addition, polypeptides can be chemically synthesized using techniques known in the art (See, *e.g.*, Creighton, 1983 Proteins. New York, N.Y.: W. H. Freeman and Company; and Hunkapiller et al., (1984) Nature July 12 -18;310(5973):105-11). For example, a relative short fragment can be synthesized by use of a peptide synthesizer. Furthermore, if desired, non-classical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the fragment sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid, a-amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, g-Abu, e-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoroamino acids, designer amino acids such as b-methyl amino acids, Ca-methyl amino acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

[0069] Polypeptides and polypeptide fragments sometimes are differentially modified during or after translation, *e.g.*, by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH4; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; and the like. Additional post-translational modifications include, for example, N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of prokaryotic host cell expression. The polypeptide fragments may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the polypeptide.

[0070] Also provided are chemically modified derivatives of polypeptides that can provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (*see e.g.*, U.S. Pat. No: 4,179,337. The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

[0071] The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between about 1 kDa and about 100 kDa (the term

"about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog).

[0072] The polymers should be attached to the polypeptide with consideration of effects on functional or antigenic domains of the polypeptide. There are a number of attachment methods available to those skilled in the art (*e.g.*, EP 0 401 384 (coupling PEG to G-CSF) and Malik et al. (1992) Exp Hematol. September;20(8):1028-35 (pegylation of GM-CSF using tresyl chloride)). For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues, glutamic acid residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. For therapeutic purposes, the attachment sometimes is at an amino group, such as attachment at the N-terminus or lysine group.

[0073] Proteins can be chemically modified at the N-terminus. Using polyethylene glycol as an illustration of such a composition, one may select from a variety of polyethylene glycol molecules (by molecular weight, branching, and the like), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus may be accomplished by reductive alkylation, which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

Substantially Identical Nucleic Acids and Polypeptides

[0074] Nucleotide sequences and polypeptide sequences that are substantially identical to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence and the target polypeptide sequences encoded by those nucleotide sequences, respectively, are included herein. The term "substantially identical" as used herein refers to two or more nucleic acids or polypeptides sharing one or more identical nucleotide sequences or polypeptide sequences, respectively. Included are nucleotide sequences or polypeptide

sequences that are 55% or more, 60% or more, 65% or more, 70% or more, 75% or more, 80% or more, 85% or more, 90% or more, 95% or more (each often within a 1%, 2%, 3% or 4% variability) identical to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence or the encoded target polypeptide amino acid sequences. One test for determining whether two nucleic acids are substantially identical is to determine the percent of identical nucleotide sequences or polypeptide sequences shared between the nucleic acids or polypeptides.

[0075] Calculations of sequence identity are often performed as follows. Sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). The length of a reference sequence aligned for comparison purposes is sometimes 30% or more, 40% or more, 50% or more, often 60% or more, and more often 70% or more, 80% or more, 90% or more, or 100% of the length of the reference sequence. The nucleotides or amino acids at corresponding nucleotide or polypeptide positions, respectively, are then compared among the two sequences. When a position in the first sequence is occupied by the same nucleotide or amino acid as the corresponding position in the second sequence, the nucleotides or amino acids are deemed to be identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, introduced for optimal alignment of the two sequences.

[0076] Comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. Percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of Meyers & Miller, *CABIOS 4:* 11-17 (1989), which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. Also, percent identity between two amino acid sequences can be determined using the Needleman & Wunsch, *J. Mol. Biol. 48:* 444-453 (1970) algorithm which has been incorporated into the GAP program in the GCG software package (available at the http address www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. Percent identity between two nucleotide sequences can be determined using the GAP program in the GCG software package (available at http address www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A set of parameters often used is a Blossum 62 scoring matrix with a gap open penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

[0077] Another manner for determining if two nucleic acids are substantially identical is to assess whether a polynucleotide homologous to one nucleic acid will hybridize to the other nucleic acid under stringent conditions. As use herein, the term "stringent conditions" refers to conditions for hybridization and washing. Stringent conditions are known to those skilled in the art and can be found in *Current*

Protocols in Molecular Biology, John Wiley & Sons, N.Y. , 6.3.1-6.3.6 (1989). Aqueous and non-aqueous methods are described in that reference and either can be used. An example of stringent hybridization conditions is hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50°C. Another example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 55°C. A further example of stringent hybridization conditions is hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 60°C. Often, stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C. More often, stringency conditions are 0.5M sodium phosphate, 7% SDS at 65°C, followed by one or more washes at 0.2X SSC, 1% SDS at 65°C.

[0078] An example of a substantially identical nucleotide sequence to a nucleotide sequence in SEQ ID NO: 1-12 is one that has a different nucleotide sequence but still encodes the same polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO: 1-12. Another example is a nucleotide sequence that encodes a polypeptide having a polypeptide sequence that is more than 70% or more identical to, sometimes more than 75% or more, 80% or more, or 85% or more identical to, and often more than 90% or more and 95% or more identical to a polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12.

[0079] Nucleotide sequences in SEQ ID NO: 1-12 and amino acid sequences of encoded polypeptides can be used as "query sequences" to perform a search against public databases to identify other family members or related sequences, for example. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul *et al., J. Mol. Biol. 215:* 403-10 (1990). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to nucleotide sequences in SEQ ID NO: 1-12. BLAST polypeptide searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to polypeptides encoded by the nucleotide sequences of SEQ ID NO: 1-12. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al., Nucleic Acids Res. 25(17):* 3389-3402 (1997). When utilizing BLAST and Gapped BLAST programs, default parameters of the respective programs (*e.g.*, XBLAST and NBLAST) can be used (*see* the http address www.ncbi.nlm.nih.gov).

[0080] A nucleic acid that is substantially identical to a nucleotide sequence in SEQ ID NO: 1 may include polymorphic sites at positions equivalent to those described herein when the sequences are aligned. For example, using the alignment procedures described herein, SNPs in a sequence substantially identical to a sequence in SEQ ID NO: 1-12 can be identified at nucleotide positions that match (*i.e.*,

align) with nucleotides at SNP positions in each nucleotide sequence in SEQ ID NO: 1-12. Also, where a polymorphic variation results in an insertion or deletion, insertion or deletion of a nucleotide sequence from a reference sequence can change the relative positions of other polymorphic sites in the nucleotide sequence.

[0081] Substantially identical nucleotide and polypeptide sequences include those that are naturally occurring, such as allelic variants (same locus), splice variants, homologs (different locus), and orthologs (different organism) or can be non-naturally occurring. Non-naturally occurring variants can be generated by mutagenesis techniques, including those applied to polynucleotides, cells, or organisms. The variants can contain nucleotide substitutions, deletions, inversions and insertions. Variation can occur in either or both the coding and non-coding regions. The variations can produce both conservative and non-conservative amino acid substitutions (as compared in the encoded product). Orthologs, homologs, allelic variants, and splice variants can be identified using methods known in the art. These variants normally comprise a nucleotide sequence encoding a polypeptide that is 50% or more, about 55% or more, often about 70-75% or more or about 80-85% or more, and sometimes about 90-95% or more identical to the amino acid sequences of target polypeptides or a fragment thereof. Such nucleic acid molecules can readily be identified as being able to hybridize under stringent conditions to a nucleotide sequence in SEQ ID NO: 1-12 or a fragment of this sequence. Nucleic acid molecules corresponding to orthologs, homologs, and allelic variants of a nucleotide sequence in SEQ ID NO: 1-12 can further be identified by mapping the sequence to the same chromosome or locus as the nucleotide sequence in SEQ ID NO: 1-12.

[0082] Also, substantially identical nucleotide sequences may include codons that are altered with respect to the naturally occurring sequence for enhancing expression of a target polypeptide in a particular expression system. For example, the nucleic acid can be one in which one or more codons are altered, and often 10% or more or 20% or more of the codons are altered for optimized expression in bacteria (*e.g.*, *E. coli*.), yeast (*e.g.*, *S. cervesiae*), human (*e.g.*, 293 cells), insect, or rodent (*e.g.*, hamster) cells.

Methods for Identifying Risk of osteoarthritis

[0083] Methods for prognosing and diagnosing osteoarthritis are included herein. These methods include detecting the presence or absence of one or more polymorphic variations in a nucleotide sequence associated with osteoarthritis, such as variants in or around the loci set forth herein, or a substantially identical sequence thereof, in a sample from a subject, where the presence of a polymorphic variant described herein is indicative of a risk of osteoarthritis. Determining a risk of osteoarthritis sometimes refers to determining whether an individual is at an increased risk of osteoarthritis (*e.g.*, intermediate risk or higher risk).

[0084] Thus, featured herein is a method for identifying a subject who is at risk of osteoarthritis, which comprises detecting an aberration associated with osteoarthritis in a nucleic acid sample from the subject. An embodiment is a method for detecting a risk of osteoarthritis in a subject, which comprises detecting the presence or absence of a polymorphic variation associated with osteoarthritis at a polymorphic site in a nucleotide sequence in a nucleic acid sample from a subject, where the nucleotide sequence comprises a polynucleotide sequence selected from the group consisting of: (a) a nucleotide sequence of SEQ ID NO: 1-12; (b) a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-12; (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-12, or a nucleotide sequence about 90% or more identical to a nucleotide sequence of SEQ ID NO: 1-12; and (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic site; whereby the presence of the polymorphic variation is indicative of a predisposition to osteoarthritis in the subject. In certain embodiments, polymorphic variants at the positions described herein are detected for determining a risk of osteoarthritis, and polymorphic variants at positions in linkage disequilibrium with these positions are detected for determining a risk of osteoarthritis. As used herein, "SEQ ID NO: 1-12" refers to individual sequences of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12, each sequence being separately applicable to embodiments described herein.

[0085] Risk of osteoarthritis sometimes is expressed as a probability, such as an odds ratio, percentage, or risk factor. Risk often is based upon the presence or absence of one or more polymorphic variants described herein, and also may be based in part upon phenotypic traits of the individual being tested. Methods for calculating risk based upon patient data are well known (*see, e.g.*, Agresti, *Categorical Data Analysis*, 2nd Ed. 2002. Wiley). Allelotyping and genotyping analyses may be carried out in populations other than those exemplified herein to enhance the predictive power of the prognostic method. These further analyses are executed in view of the exemplified procedures described herein, and may be based upon the same polymorphic variations or additional polymorphic variations.

[0086] In certain embodiments, determining the presence of a combination of two or more polymorphic variants associated with osteoarthritis in one or more genetic loci (e.g., one or more genes) of the sample is determined to identify, quantify and/or estimate, risk of osteoarthritis. The risk often is the probability of having or developing osteoarthritis. The risk sometimes is expressed as a relative risk with respect to a population average risk of osteoarthritis, and sometimes is expressed as a relative risk with respect to the lowest risk group. Such relative risk assessments often are based upon penetrance values determined by statistical methods, and are particularly useful to clinicians and insurance companies for assessing risk of osteoarthritis (e.g., a clinician can target appropriate detection, prevention and therapeutic regimens to a patient after determining the patient's risk of osteoarthritis, and an insurance company can fine tune actuarial tables based upon population genotype assessments of

osteoarthritis risk). Risk of osteoarthritis sometimes is expressed as an odds ratio, which is the odds of a particular person having a genotype has or will develop osteoarthritis with respect to another genotype group (e.g., the most disease protective genotype or population average). In related embodiments, the determination is utilized to identify a subject at risk of osteoarthritis. In an embodiment, two or more polymorphic variations are detected in two or more regions in human genomic DNA associated with increased risk of osteoarthritis, such as a locus containing a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG*, for example. In certain embodiments, 3 or more, or 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 or more polymorphic variants are detected in the sample. In specific embodiments, polymorphic variants are detected in a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* region, for example. In another embodiment, polymorphic variants are detected at two or more positions selected from the group consisting of rs756519, rs1042327, rs8770, rs1563055, rs912428 and rs1888475; 229, 16559, 44850 and/or 46252 in SEQ ID NO: 1; 40985, 46168, 51925 and/or 52168 in SEQ ID NO: 2; 49693, 82475, 92462 and/or 96275 in SEQ ID NO: 3; and 33137, 55499 and/or 58282 in SEQ ID NO: 4. In certain embodiments, polymorphic variants are detected at other genetic loci (e.g., the polymorphic variants can be detected in *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* in addition to other loci or only in other loci), where the other loci include but are not limited to those described in concurrently-filed patent applications having attorney docket number 524593008800, 524593008900, 524593009000, 524593009100 or 524593009200, each of which is incorporated herein by reference in its entirety.

[0087] Results from prognostic tests may be combined with other test results to diagnose osteoarthritis. For example, prognostic results may be gathered, a patient sample may be ordered based on a determined predisposition to osteoarthritis, the patient sample is analyzed, and the results of the analysis may be utilized to diagnose osteoarthritis. Also osteoarthritis diagnostic method can be developed from studies used to generate prognostic methods in which populations are stratified into subpopulations having different progressions of osteoarthritis. In another embodiment, prognostic results may be gathered, a patient's risk factors for developing osteoarthritis (*e.g.*, age, weight, race, diet) analyzed, and a patient sample may be ordered based on a determined predisposition to osteoarthritis.

[0088] The nucleic acid sample typically is isolated from a biological sample obtained from a subject. For example, nucleic acid can be isolated from blood, saliva, sputum, urine, cell scrapings, and biopsy tissue. The nucleic acid sample can be isolated from a biological sample using standard techniques, such as the technique described in Example 2. As used herein, the term "subject" refers primarily to humans but also refers to other mammals such as dogs, cats, and ungulates (*e.g.*, cattle, sheep, and swine). Subjects also include avians (*e.g.*, chickens and turkeys), reptiles, and fish (*e.g.*, salmon), as embodiments described herein can be adapted to nucleic acid samples isolated from any of these organisms. The nucleic acid sample may be isolated from the subject and then directly utilized in a

method for determining the presence of a polymorphic variant, or alternatively, the sample may be isolated and then stored (*e.g.*, frozen) for a period of time before being subjected to analysis.

[0089] The presence or absence of a polymorphic variant is determined using one or both chromosomal complements represented in the nucleic acid sample. Determining the presence or absence of a polymorphic variant in both chromosomal complements represented in a nucleic acid sample from a subject having a copy of each chromosome is useful for determining the zygosity of an individual for the polymorphic variant (*i.e.*, whether the individual is homozygous or heterozygous for the polymorphic variant). Any oligonucleotide-based diagnostic may be utilized to determine whether a sample includes the presence or absence of a polymorphic variant in a sample. For example, primer extension methods, ligase sequence determination methods (*e.g.*, U.S. Pat. Nos. 5,679,524 and 5,952,174, and WO 01/27326), mismatch sequence determination methods (*e.g.*, U.S. Pat. Nos. 5,851,770; 5,958,692; 6,110,684; and 6,183,958), microarray sequence determination methods, restriction fragment length polymorphism (RFLP), single strand conformation polymorphism detection (SSCP) (*e.g.*, U.S. Pat. Nos. 5,891,625 and 6,013,499), PCR-based assays (*e.g.*, TAQMAN® PCR System (Applied Biosystems)), and nucleotide sequencing methods may be used.

[0090] Oligonucleotide extension methods typically involve providing a pair of oligonucleotide primers in a polymerase chain reaction (PCR) or in other nucleic acid amplification methods for the purpose of amplifying a region from the nucleic acid sample that comprises the polymorphic variation. One oligonucleotide primer is complementary to a region 3' of the polymorphism and the other is complementary to a region 5' of the polymorphism. A PCR primer pair may be used in methods disclosed in U.S. Pat. Nos. 4,683,195; 4,683,202, 4,965,188; 5,656,493; 5,998,143; 6,140,054; WO 01/27327; and WO 01/27329 for example. PCR primer pairs may also be used in any commercially available machines that perform PCR, such as any of the GENEAMP® Systems available from Applied Biosystems. Also, those of ordinary skill in the art will be able to design oligonucleotide primers based upon a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence using knowledge available in the art.

[0091] Also provided is an extension oligonucleotide that hybridizes to the amplified fragment adjacent to the polymorphic variation. As used herein, the term "adjacent" refers to the 3' end of the extension oligonucleotide being often 1 nucleotide from the 5' end of the polymorphic site, and sometimes 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides from the 5' end of the polymorphic site, in the nucleic acid when the extension oligonucleotide is hybridized to the nucleic acid. The extension oligonucleotide then is extended by one or more nucleotides, and the number and/or type of nucleotides that are added to the extension oligonucleotide determine whether the polymorphic variant is present. Oligonucleotide extension methods are disclosed, for example, in U.S. Pat. Nos. 4,656,127; 4,851,331; 5,679,524; 5,834,189; 5,876,934; 5,908,755; 5,912,118; 5,976,802; 5,981,186; 6,004,744; 6,013,431; 6,017,702;

6,046,005; 6,087,095; 6,210,891; and WO 01/20039. Oligonucleotide extension methods using mass spectrometry are described, for example, in U.S. Pat. Nos. 5,547,835; 5,605,798; 5,691,141; 5,849,542; 5,869,242; 5,928,906; 6,043,031; and 6,194,144, and a method often utilized is described herein in Example 2.

[0092] A microarray can be utilized for determining whether a polymorphic variant is present or absent in a nucleic acid sample. A microarray may include any oligonucleotides described herein, and methods for making and using oligonucleotide microarrays suitable for diagnostic use are disclosed in U.S. Pat. Nos. 5,492,806; 5,525,464; 5,589,330; 5,695,940; 5,849,483; 6,018,041; 6,045,996; 6,136,541; 6,142,681; 6,156,501; 6,197,506; 6,223,127; 6,225,625; 6,229,911; 6,239,273; WO 00/52625; WO 01/25485; and WO 01/29259. The microarray typically comprises a solid support and the oligonucleotides may be linked to this solid support by covalent bonds or by non-covalent interactions. The oligonucleotides may also be linked to the solid support directly or by a spacer molecule. A microarray may comprise one or more oligonucleotides complementary to a polymorphic site set forth herein.

[0093] A kit also may be utilized for determining whether a polymorphic variant is present or absent in a nucleic acid sample. A kit often comprises one or more pairs of oligonucleotide primers useful for amplifying a fragment of a nucleotide sequence of SEQ ID NO: 1-12 or a substantially identical sequence thereof, where the fragment includes a polymorphic site. The kit sometimes comprises a polymerizing agent, for example, a thermostable nucleic acid polymerase such as one disclosed in U.S. Pat. Nos. 4,889,818 or 6,077,664. Also, the kit often comprises an elongation oligonucleotide that hybridizes to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence in a nucleic acid sample adjacent to the polymorphic site. Where the kit includes an elongation oligonucleotide, it also often comprises chain elongating nucleotides, such as dATP, dTTP, dGTP, dCTP, and dITP, including analogs of dATP, dTTP, dGTP, dCTP and dITP, provided that such analogs are substrates for a thermostable nucleic acid polymerase and can be incorporated into a nucleic acid chain elongated from the extension oligonucleotide. Along with chain elongating nucleotides would be one or more chain terminating nucleotides such as ddATP, ddTTP, ddGTP, ddCTP, and the like. In an embodiment, the kit comprises one or more oligonucleotide primer pairs, a polymerizing agent, chain elongating nucleotides, at least one elongation oligonucleotide, and one or more chain terminating nucleotides. Kits optionally include buffers, vials, microtiter plates, and instructions for use.

[0094] An individual identified as being at risk of osteoarthritis may be heterozygous or homozygous with respect to the allele associated with a higher risk of osteoarthritis. A subject homozygous for an allele associated with an increased risk of osteoarthritis is at a comparatively high risk of osteoarthritis, a subject heterozygous for an allele associated with an increased risk of osteoarthritis is at a comparatively intermediate risk of osteoarthritis, and a subject homozygous for an

allele associated with a decreased risk of osteoarthritis is at a comparatively low risk of osteoarthritis. A genotype may be assessed for a complementary strand, such that the complementary nucleotide at a particular position is detected.

[0095] Also featured are methods for determining risk of osteoarthritis and/or identifying a subject at risk of osteoarthritis by contacting a polypeptide or protein encoded by a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence from a subject with an antibody that specifically binds to an epitope associated with increased risk of osteoarthritis in the polypeptide.

Applications of Prognostic and Diagnostic Results to Pharmacogenomic Methods

[0096] Pharmacogenomics is a discipline that involves tailoring a treatment for a subject according to the subject's genotype as a particular treatment regimen may exert a differential effect depending upon the subject's genotype. For example, based upon the outcome of a prognostic test described herein, a clinician or physician may target pertinent information and preventative or therapeutic treatments to a subject who would be benefited by the information or treatment and avoid directing such information and treatments to a subject who would not be benefited (*e.g.*, the treatment has no therapeutic effect and/or the subject experiences adverse side effects).

[0097] The following is an example of a pharmacogenomic embodiment. A particular treatment regimen can exert a differential effect depending upon the subject's genotype. Where a candidate therapeutic exhibits a significant interaction with a major allele and a comparatively weak interaction with a minor allele (*e.g.*, an order of magnitude or greater difference in the interaction), such a therapeutic typically would not be administered to a subject genotyped as being homozygous for the minor allele, and sometimes not administered to a subject genotyped as being heterozygous for the minor allele. In another example, where a candidate therapeutic is not significantly toxic when administered to subjects who are homozygous for a major allele but is comparatively toxic when administered to subjects heterozygous or homozygous for a minor allele, the candidate therapeutic is not typically administered to subjects who are genotyped as being heterozygous or homozygous with respect to the minor allele.

[0098] The methods described herein are applicable to pharmacogenomic methods for preventing, alleviating or treating osteoarthritis. For example, a nucleic acid sample from an individual may be subjected to a prognostic test described herein. Where one or more polymorphic variations associated with increased risk of osteoarthritis are identified in a subject, information for preventing or treating osteoarthritis and/or one or more osteoarthritis treatment regimens then may be prescribed to that subject.

[0099] In certain embodiments, a treatment or preventative regimen is specifically prescribed and/or administered to individuals who will most benefit from it based upon their risk of developing osteoarthritis assessed by the methods described herein. Thus, provided are methods for identifying a subject predisposed to osteoarthritis and then prescribing a therapeutic or preventative regimen to

individuals identified as having a predisposition. Thus, certain embodiments are directed to a method for reducing osteoarthritis in a subject, which comprises: detecting the presence or absence of a polymorphic variant associated with osteoarthritis in a nucleotide sequence in a nucleic acid sample from a subject, where the nucleotide sequence comprises a polynucleotide sequence selected from the group consisting of: (a) a nucleotide sequence of SEQ ID NO: 1-12; (b) a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-12; (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-12, or a nucleotide sequence about 90% or more identical to a nucleotide sequence of SEQ ID NO: 1-12; and (d) a fragment of a polynucleotide sequence of (a), (b), or (c); and prescribing or administering a treatment regimen to a subject from whom the sample originated where the presence of a polymorphic variation associated with osteoarthritis is detected in the nucleotide sequence. In these methods, predisposition results may be utilized in combination with other test results to diagnose osteoarthritis.

[0100] Certain preventative treatments often are prescribed to subjects having a predisposition to osteoarthritis and where the subject is diagnosed with osteoarthritis or is diagnosed as having symptoms indicative of an early stage of osteoarthritis. The treatment sometimes is preventative (*e.g.*, is prescribed or administered to reduce the probability that osteoarthritis arises or progresses), sometimes is therapeutic, and sometimes delays, alleviates or halts the progression of osteoarthritis. Any known preventative or therapeutic treatment for alleviating or preventing the occurrence of osteoarthritis is prescribed and/or administered. For example, the treatment often is directed to decreasing pain and improving joint movement. Examples of OA treatments include exercises to keep joints flexible and improve muscle strength. Different medications to control pain, including corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs, e.g., Voltaren); cyclooxygenase-2 (COX-2) inhibitors (e.g., Celebrex, Vioxx, Mobic, and Bextra); monoclonal antibodies (e.g., Remicade); tumor necrosis factor inhibitors (e.g., Enbrel); or injections of glucocorticoids, hyaluronic acid or chondrotin sulfate into joints that are inflamed and not responsive to NSAIDS. Orally administered chondroitin sulfate also may be used as a therapeutic, as it may increase hyaluronic acid levels and viscosity of synovial fluid, and decrease collagenase levels in synovial fluid. Also, glucosamine can serve as an OA therapeutic as delivering it into joints may inhibit enzymes involved in cartilage degradation and enhance the production of hyaluronic acid. For mild pain without inflammation, acetaminophen may be used. Other treatments include: heat/cold therapy for temporary pain relief; joint protection to prevent strain or stress on painful joints; surgery to relieve chronic pain in damaged joints; and weight control to prevent extra stress on weight-bearing joints.

[0101] As therapeutic approaches for treating osteoarthritis continue to evolve and improve, the goal of treatments for osteoarthritis related disorders is to intervene even before clinical signs first manifest.

Thus, genetic markers associated with susceptibility to osteoarthritis prove useful for early diagnosis, prevention and treatment of osteoarthritis.

[0102] As osteoarthritis preventative and treatment information can be specifically targeted to subjects in need thereof (*e.g.*, those at risk of developing osteoarthritis or those in an early stage of osteoarthritis), provided herein is a method for preventing or reducing the risk of developing osteoarthritis in a subject, which comprises: (a) detecting the presence or absence of a polymorphic variation associated with osteoarthritis at a polymorphic site in a nucleotide sequence in a nucleic acid sample from a subject; (b) identifying a subject with a predisposition to osteoarthritis, whereby the presence of the polymorphic variation is indicative of a predisposition to osteoarthritis in the subject; and (c) if such a predisposition is identified, providing the subject with information about methods or products to prevent or reduce osteoarthritis or to delay the onset of osteoarthritis. Also provided is a method of targeting information or advertising to a subpopulation of a human population based on the subpopulation being genetically predisposed to a disease or condition, which comprises: (a) detecting the presence or absence of a polymorphic variation associated with osteoarthritis at a polymorphic site in a nucleotide sequence in a nucleic acid sample from a subject; (b) identifying the subpopulation of subjects in which the polymorphic variation is associated with osteoarthritis; and (c) providing information only to the subpopulation of subjects about a particular product which may be obtained and consumed or applied by the subject to help prevent or delay onset of the disease or condition.

[0103] Pharmacogenomics methods also may be used to analyze and predict a response to osteoarthritis treatment or a drug. For example, if pharmacogenomics analysis indicates a likelihood that an individual will respond positively to osteoarthritis treatment with a particular drug, the drug may be administered to the individual. Conversely, if the analysis indicates that an individual is likely to respond negatively to treatment with a particular drug, an alternative course of treatment may be prescribed. A negative response may be defined as either the absence of an efficacious response or the presence of toxic side effects. The response to a therapeutic treatment can be predicted in a background study in which subjects in any of the following populations are genotyped: a population that responds favorably to a treatment regimen, a population that does not respond significantly to a treatment regimen, and a population that responds adversely to a treatment regimen (*e.g.*, exhibits one or more side effects). These populations are provided as examples and other populations and subpopulations may be analyzed. Based upon the results of these analyses, a subject is genotyped to predict whether he or she will respond favorably to a treatment regimen, not respond significantly to a treatment regimen, or respond adversely to a treatment regimen.

[0104] The tests described herein also are applicable to clinical drug trials. One or more polymorphic variants indicative of response to an agent for treating osteoarthritis or to side effects to an agent for treating osteoarthritis may be identified using the methods described herein. Thereafter,

potential participants in clinical trials of such an agent may be screened to identify those individuals most likely to respond favorably to the drug and exclude those likely to experience side effects. In that way, the effectiveness of drug treatment may be measured in individuals who respond positively to the drug, without lowering the measurement as a result of the inclusion of individuals who are unlikely to respond positively in the study and without risking undesirable safety problems.

[0105] Thus, another embodiment is a method of selecting an individual for inclusion in a clinical trial of a treatment or drug comprising the steps of: (a) obtaining a nucleic acid sample from an individual; (b) determining the identity of a polymorphic variation which is associated with a positive response to the treatment or the drug, or at least one polymorphic variation which is associated with a negative response to the treatment or the drug in the nucleic acid sample, and (c) including the individual in the clinical trial if the nucleic acid sample contains said polymorphic variation associated with a positive response to the treatment or the drug or if the nucleic acid sample lacks said polymorphic variation associated with a negative response to the treatment or the drug. In addition, the methods described herein for selecting an individual for inclusion in a clinical trial of a treatment or drug encompass methods with any further limitation described in this disclosure, or those following, specified alone or in any combination. The polymorphic variation may be in a sequence selected individually or in any combination from the group consisting of (i) a nucleotide sequence of SEQ ID NO: 1-12; (ii) a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-12; (iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-12, or a nucleotide sequence about 90% or more identical to a nucleotide sequence of SEQ ID NO: 1-12; and (iv) a fragment of a polynucleotide sequence of (i), (ii), or (iii) comprising the polymorphic site. The including step (c) optionally comprises administering the drug or the treatment to the individual if the nucleic acid sample contains the polymorphic variation associated with a positive response to the treatment or the drug and the nucleic acid sample lacks said biallelic marker associated with a negative response to the treatment or the drug.

[0106] Also provided herein is a method of partnering between a diagnostic/prognostic testing provider and a provider of a consumable product, which comprises: (a) the diagnostic/prognostic testing provider detects the presence or absence of a polymorphic variation associated with osteoarthritis at a polymorphic site in a nucleotide sequence in a nucleic acid sample from a subject; (b) the diagnostic/prognostic testing provider identifies the subpopulation of subjects in which the polymorphic variation is associated with osteoarthritis; (c) the diagnostic/prognostic testing provider forwards information to the subpopulation of subjects about a particular product which may be obtained and consumed or applied by the subject to help prevent or delay onset of the disease or condition; and (d) the

provider of a consumable product forwards to the diagnostic test provider a fee every time the diagnostic/prognostic test provider forwards information to the subject as set forth in step (c) above.

Compositions Comprising Osteoarthritis-Directed Molecules

[0107] Featured herein is a composition comprising a cell from a subject having osteoarthritis or at risk of osteoarthritis and one or more molecules specifically directed and targeted to a nucleic acid comprising a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence or amino acid sequence. Such directed molecules include, but are not limited to, a compound that binds to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence or amino acid sequence referenced herein; a RNAi or siRNA molecule having a strand complementary or substantially complementary to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence (e.g., hybridizes to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence under conditions of high stringency); an antisense nucleic acid complementary or substantially complementary to an RNA encoded by a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence (e.g., hybridizes to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence under conditions of high stringency); a ribozyme that hybridizes to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence (e.g., hybridizes to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence under conditions of high stringency); a nucleic acid aptamer that specifically binds a polypeptide encoded by *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence; and an antibody that specifically binds to a polypeptide encoded by *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence or binds to a nucleic acid having such a nucleotide sequence. In specific embodiments, the osteoarthritis directed molecule interacts with a nucleic acid or polypeptide variant associated with osteoarthritis, such as variants referenced herein. In other embodiments, the osteoarthritis directed molecule interacts with a polypeptide involved in a signal pathway of a polypeptide encoded by a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence, or a nucleic acid comprising such a nucleotide sequence.

[0108] Compositions sometimes include an adjuvant known to stimulate an immune response, and in certain embodiments, an adjuvant that stimulates a T-cell lymphocyte response. Adjuvants are known, including but not limited to an aluminum adjuvant (e.g., aluminum hydroxide); a cytokine adjuvant or adjuvant that stimulates a cytokine response (e.g., interleukin (IL)-12 and/or gamma-interferon cytokines); a Freund-type mineral oil adjuvant emulsion (e.g., Freund's complete or incomplete adjuvant); a synthetic lipoid compound; a copolymer adjuvant (e.g., TitreMax); a saponin; Quil A; a liposome; an oil-in-water emulsion (e.g., an emulsion stabilized by Tween 80 and pluronic polyoxyethlene/polyoxypropylene block copolymer (Syntex Adjuvant Formulation); TitreMax; detoxified endotoxin (MPL) and mycobacterial cell wall components (TDW, CWS) in 2% squalene (Ribi Adjuvant System)); a muramyl dipeptide; an immune-stimulating complex (ISCOM, e.g., an Ag-

modified saponin/cholesterol micelle that forms stable cage-like structure); an aqueous phase adjuvant that does not have a depot effect (e.g., Gerbu adjuvant); a carbohydrate polymer (e.g., AdjuPrime); L-tyrosine; a manide-oleate compound (e.g., Montanide); an ethylene-vinyl acetate copolymer (e.g., Elvax 40W1,2); or lipid A, for example. Such compositions are useful for generating an immune response against osteoarthritis directed molecule (e.g., an HLA-binding subsequence within a polypeptide encoded by a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence). In such methods, a peptide having an amino acid subsequence of a polypeptide encoded by a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence is delivered to a subject, where the subsequence binds to an HLA molecule and induces a CTL lymphocyte response. The peptide sometimes is delivered to the subject as an isolated peptide or as a minigene in a plasmid that encodes the peptide. Methods for identifying HLA-binding subsequences in such polypeptides are known (see e.g., publication WO02/20616 and PCT application US98/01373 for methods of identifying such sequences).

[0109] The cell may be in a group of cells cultured *in vitro* or in a tissue maintained *in vitro* or present in an animal *in vivo* (e.g., a rat, mouse, ape or human). In certain embodiments, a composition comprises a component from a cell such as a nucleic acid molecule (e.g., genomic DNA), a protein mixture or isolated protein, for example. The aforementioned compositions have utility in diagnostic, prognostic and pharmacogenomic methods described previously and in therapeutics described hereafter. Certain osteoarthritis directed molecules are described in greater detail below.

Compounds

[0110] Compounds can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; peptoid libraries (libraries of molecules having the functionalities of peptides, but with a novel, non-peptide backbone which are resistant to enzymatic degradation but which nevertheless remain bioactive (see, e.g., Zuckermann et al., J. Med. Chem.37: 2678-85 (1994)); spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; "one-bead one-compound" library methods; and synthetic library methods using affinity chromatography selection. Biological library and peptoid library approaches are typically limited to peptide libraries, while the other approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds (Lam, Anticancer Drug Des. 12: 145, (1997)). Examples of methods for synthesizing molecular libraries are described, for example, in DeWitt et al., Proc. Natl. Acad. Sci. U.S.A. 90: 6909 (1993); Erb et al., Proc. Natl. Acad. Sci. USA 91: 11422 (1994); Zuckermann et al., J. Med. Chem. 37: 2678 (1994); Cho et al., Science 261: 1303 (1993); Carrell et al., Angew. Chem. Int. Ed. Engl. 33: 2059 (1994); Carell et al., Angew. Chem. Int. Ed. Engl. 33: 2061 (1994); and in Gallop et al., J. Med. Chem. 37: 1233 (1994).

[0111] Libraries of compounds may be presented in solution (e.g., Houghten, Biotechniques 13: 412-421 (1992)), or on beads (Lam, Nature 354: 82-84 (1991)), chips (Fodor, Nature 364: 555-556 (1993)), bacteria or spores (Ladner, United States Patent No. 5,223,409), plasmids (Cull et al., Proc. Natl. Acad. Sci. USA 89: 1865-1869 (1992)) or on phage (Scott and Smith, Science 249: 386-390 (1990); Devlin, Science 249: 404-406 (1990); Cwirla et al., Proc. Natl. Acad. Sci. 87: 6378-6382 (1990); Felici, J. Mol. Biol. 222: 301-310 (1991); Ladner supra.).

[0112] A compound sometimes alters expression and sometimes alters activity of a polypeptide target and may be a small molecule. Small molecules include, but are not limited to, peptides, peptidomimetics (e.g., peptoids), amino acids, amino acid analogs, polynucleotides, polynucleotide analogs, nucleotides, nucleotide analogs, organic or inorganic compounds (i.e., including heteroorganic and organometallic compounds) having a molecular weight less than about 10,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 5,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 1,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 500 grams per mole, and salts, esters, and other pharmaceutically acceptable forms of such compounds.

Antisense Nucleic Acid Molecules, Ribozymes, RNAi, siRNA and Modified Nucleic Acid Molecules

[0113] An "antisense" nucleic acid refers to a nucleotide sequence complementary to a "sense" nucleic acid encoding a polypeptide, e.g., complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. The antisense nucleic acid can be complementary to an entire coding strand, or to a portion thereof or a substantially identical sequence thereof. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence (e.g., 5' and 3' untranslated regions in SEQ ID NO: 1).

[0114] An antisense nucleic acid can be designed such that it is complementary to the entire coding region of an mRNA encoded by a nucleotide sequence (e.g., SEQ ID NO: 1), and often the antisense nucleic acid is an oligonucleotide antisense to only a portion of a coding or noncoding region of the mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of the mRNA, e.g., between the -10 and +10 regions of the target gene nucleotide sequence of interest. An antisense oligonucleotide can be, for example, about 7, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, or more nucleotides in length. The antisense nucleic acids, which include the ribozymes described hereafter, can be designed to target a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence, often a variant associated with osteoarthritis, or a substantially identical sequence thereof. Among the variants, minor alleles and major alleles can be targeted, and

those associated with a higher risk of osteoarthritis are often designed, tested, and administered to subjects.

[0115] An antisense nucleic acid can be constructed using chemical synthesis and enzymatic ligation reactions using standard procedures. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. Antisense nucleic acid also can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

[0116] When utilized as therapeutics, antisense nucleic acids typically are administered to a subject (e.g., by direct injection at a tissue site) or generated in situ such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a polypeptide and thereby inhibit expression of the polypeptide, for example, by inhibiting transcription and/or translation. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then are administered systemically. For systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, for example, by linking antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. Antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. Sufficient intracellular concentrations of antisense molecules are achieved by incorporating a strong promoter, such as a pol II or pol III promoter, in the vector construct.

[0117] Antisense nucleic acid molecules sometimes are alpha-anomeric nucleic acid molecules. An alpha-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual beta-units, the strands run parallel to each other (Gaultier et al., Nucleic Acids. Res. 15: 6625-6641 (1987)). Antisense nucleic acid molecules can also comprise a 2'-o-methylribonucleotide (Inoue et al., Nucleic Acids Res. 15: 6131-6148 (1987)) or a chimeric RNA-DNA analogue (Inoue et al., FEBS Lett. 215: 327-330 (1987)). Antisense nucleic acids sometimes are composed of DNA or PNA or any other nucleic acid derivatives described previously.

[0118] In another embodiment, an antisense nucleic acid is a ribozyme. A ribozyme having specificity for a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence can include one or more sequences complementary to such a nucleotide sequence, and a sequence having a known catalytic region responsible for mRNA cleavage (see e.g., U.S. Pat. No. 5,093,246 or Haselhoff and Gerlach, Nature 334: 585-591 (1988)). For example, a derivative of a Tetrahymena L-19 IVS RNA is sometimes utilized in which the nucleotide sequence of the active site is complementary to the nucleotide sequence

to be cleaved in a mRNA (see e.g., Cech et al. U.S. Patent No. 4,987,071; and Cech et al. U.S. Patent No. 5,116,742). Also, target mRNA sequences can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules (see e.g., Bartel & Szostak, Science 261: 1411-1418 (1993)).

[0119] Osteoarthritis directed molecules include in certain embodiments nucleic acids that can form triple helix structures with a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence, or a substantially identical sequence thereof, especially one that includes a regulatory region that controls expression of a polypeptide. Gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of a nucleotide sequence referenced herein or a substantially identical sequence (e.g., promoter and/or enhancers) to form triple helical structures that prevent transcription of a gene in target cells (see e.g., Helene, Anticancer Drug Des. 6(6): 569-84 (1991); Helene et al., Ann. N.Y. Acad. Sci. 660: 27-36 (1992); and Maher, Bioassays 14(12): 807-15 (1992). Potential sequences that can be targeted for triple helix formation can be increased by creating a so-called "switchback" nucleic acid molecule. Switchback molecules are synthesized in an alternating 5'-3', 3'-5' manner, such that they base pair with first one strand of a duplex and then the other, eliminating the necessity for a sizeable stretch of either purines or pyrimidines to be present on one strand of a duplex.

[0120] Osteoarthritis directed molecules include RNAi and siRNA nucleic acids. Gene expression may be inhibited by the introduction of double-stranded RNA (dsRNA), which induces potent and specific gene silencing, a phenomenon called RNA interference or RNAi. See, e.g., Fire et al., US Patent Number 6,506,559; Tuschl et al. PCT International Publication No. WO 01/75164; Kay et al. PCT International Publication No. WO 03/010180A1; or Bosher JM, Labouesse, Nat Cell Biol 2000 Feb;2(2):E31-6. This process has been improved by decreasing the size of the double-stranded RNA to 20-24 base pairs (to create small-interfering RNAs or siRNAs) that "switched off" genes in mammalian cells without initiating an acute phase response, i.e., a host defense mechanism that often results in cell death (see, e.g., Caplen et al. Proc Natl Acad Sci U S A. 2001 Aug 14;98(17):9742-7 and Elbashir et al. Methods 2002 Feb;26(2):199-213). There is increasing evidence of post-transcriptional gene silencing by RNA interference (RNAi) for inhibiting targeted expression in mammalian cells at the mRNA level, in human cells. There is additional evidence of effective methods for inhibiting the proliferation and migration of tumor cells in human patients, and for inhibiting metastatic cancer development (see, e.g., U.S. Patent Application No. US2001000993183; Caplen et al. Proc Natl Acad Sci U S A; and Abderrahmani et al. Mol Cell Biol 2001 Nov21(21):7256-67).

[0121] An "siRNA" or "RNAi" refers to a nucleic acid that forms a double stranded RNA and has the ability to reduce or inhibit expression of a gene or target gene when the siRNA is delivered to or expressed in the same cell as the gene or target gene. "siRNA" refers to short double-stranded RNA formed by the complementary strands. Complementary portions of the siRNA that hybridize to form the

double stranded molecule often have substantial or complete identity to the target molecule sequence. In one embodiment, an siRNA refers to a nucleic acid that has substantial or complete identity to a target gene and forms a double stranded siRNA.

[0122] When designing the siRNA molecules, the targeted region often is selected from a given DNA sequence beginning 50 to 100 nucleotides downstream of the start codon. See, e.g., Elbashir et al,. Methods 26:199-213 (2002). Initially, 5' or 3' UTRs and regions nearby the start codon were avoided assuming that UTR-binding proteins and/or translation initiation complexes may interfere with binding of the siRNP or RISC endonuclease complex. Sometimes regions of the target 23 nucleotides in length conforming to the sequence motif AA(N19)TT (N, an nucleotide), and regions with approximately 30% to 70% G/C-content (often about 50% G/C-content) often are selected. If no suitable sequences are found, the search often is extended using the motif NA(N21). The sequence of the sense siRNA sometimes corresponds to (N19) TT or N21 (position 3 to 23 of the 23-nt motif), respectively. In the latter case, the 3' end of the sense siRNA often is converted to TT. The rationale for this sequence conversion is to generate a symmetric duplex with respect to the sequence composition of the sense and antisense 3' overhangs. The antisense siRNA is synthesized as the complement to position 1 to 21 of the 23-nt motif. Because position 1 of the 23-nt motif is not recognized sequence-specifically by the antisense siRNA, the 3'-most nucleotide residue of the antisense siRNA can be chosen deliberately. However, the penultimate nucleotide of the antisense siRNA (complementary to position 2 of the 23-nt motif) often is complementary to the targeted sequence. For simplifying chemical synthesis, TT often is utilized. siRNAs corresponding to the target motif NAR(N17)YNN, where R is purine (A,G) and Y is pyrimidine (C,U), often are selected. Respective 21 nucleotide sense and antisense siRNAs often begin with a purine nucleotide and can also be expressed from pol III expression vectors without a change in targeting site. Expression of RNAs from pol III promoters often is efficient when the first transcribed nucleotide is a purine.

[0123] The sequence of the siRNA can correspond to the full length target gene, or a subsequence thereof. Often, the siRNA is about 15 to about 50 nucleotides in length (e.g., each complementary sequence of the double stranded siRNA is 15-50 nucleotides in length, and the double stranded siRNA is about 15-50 base pairs in length, sometimes about 20-30 nucleotides in length or about 20-25 nucleotides in length, e.g., 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. The siRNA sometimes is about 21 nucleotides in length. Methods of using siRNA are well known in the art, and specific siRNA molecules may be purchased from a number of companies including Dharmacon Research, Inc.

[0124] Antisense, ribozyme, RNAi and siRNA nucleic acids can be altered to form modified nucleic acid molecules. The nucleic acids can be altered at base moieties, sugar moieties or phosphate backbone moieties to improve stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of nucleic acid molecules can be modified to generate peptide nucleic acids (see

Hyrup et al., Bioorganic & Medicinal Chemistry 4 (1): 5-23 (1996)). As used herein, the terms "peptide nucleic acid" or "PNA" refers to a nucleic acid mimic such as a DNA mimic, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of a PNA can allow for specific hybridization to DNA and RNA under conditions of low ionic strength. Synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described, for example, in Hyrup et al., (1996) supra and Perry-O'Keefe et al., Proc. Natl. Acad. Sci. 93: 14670-675 (1996).

[0125] PNA nucleic acids can be used in prognostic, diagnostic, and therapeutic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, for example, inducing transcription or translation arrest or inhibiting replication. PNA nucleic acid molecules can also be used in the analysis of single base pair mutations in a gene, (e.g., by PNA-directed PCR clamping); as "artificial restriction enzymes" when used in combination with other enzymes, (e.g., S1 nucleases (Hyrup (1996) supra)); or as probes or primers for DNA sequencing or hybridization (Hyrup et al., (1996) supra; Perry-O'Keefe supra).

[0126] In other embodiments, oligonucleotides may include other appended groups such as peptides (e.g., for targeting host cell receptors in vivo), or agents facilitating transport across cell membranes (see e.g., Letsinger et al., Proc. Natl. Acad. Sci. USA 86: 6553-6556 (1989); Lemaitre et al., Proc. Natl. Acad. Sci. USA 84: 648-652 (1987); PCT Publication No. W088/09810) or the blood-brain barrier (see, e.g., PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (See, e.g., Krol et al., Bio-Techniques 6: 958-976 (1988)) or intercalating agents. (See, e.g., Zon, Pharm. Res. 5: 539-549 (1988)). To this end, the oligonucleotide may be conjugated to another molecule, (e.g., a peptide, hybridization triggered cross-linking agent, transport agent, or hybridization-triggered cleavage agent).

[0127] Also included herein are molecular beacon oligonucleotide primer and probe molecules having one or more regions complementary to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence, or a substantially identical sequence thereof, two complementary regions one having a fluorophore and one a quencher such that the molecular beacon is useful for quantifying the presence of the nucleic acid in a sample. Molecular beacon nucleic acids are described, for example, in Lizardi et al., U.S. Patent No. 5,854,033; Nazarenko et al., U.S. Patent No. 5,866,336, and Livak et al., U.S. Patent 5,876,930.

Antibodies

[0128] The term "antibody" as used herein refers to an immunoglobulin molecule or immunologically active portion thereof, i.e., an antigen-binding portion. Examples of immunologically active portions of immunoglobulin molecules include F(ab) and $F(ab')_2$ fragments which can be

generated by treating the antibody with an enzyme such as pepsin. An antibody sometimes is a polyclonal, monoclonal, recombinant (e.g., a chimeric or humanized), fully human, non-human (e.g., murine), or a single chain antibody. An antibody may have effector function and can fix complement, and is sometimes coupled to a toxin or imaging agent.

[0129] A full-length polypeptide or antigenic peptide fragment encoded by a nucleotide sequence referenced herein can be used as an immunogen or can be used to identify antibodies made with other immunogens, e.g., cells, membrane preparations, and the like. An antigenic peptide often includes at least 8 amino acid residues of the amino acid sequences encoded by a nucleotide sequence referenced herein, or substantially identical sequence thereof, and encompasses an epitope. Antigenic peptides sometimes include 10 or more amino acids, 15 or more amino acids, 20 or more amino acids, or 30 or more amino acids. Hydrophilic and hydrophobic fragments of polypeptides sometimes are used as immunogens.

[0130] Epitopes encompassed by the antigenic peptide are regions located on the surface of the polypeptide (e.g., hydrophilic regions) as well as regions with high antigenicity. For example, an Emini surface probability analysis of the human polypeptide sequence can be used to indicate the regions that have a particularly high probability of being localized to the surface of the polypeptide and are thus likely to constitute surface residues useful for targeting antibody production. The antibody may bind an epitope on any domain or region on polypeptides described herein.

[0131] Also, chimeric, humanized, and completely human antibodies are useful for applications which include repeated administration to subjects. Chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, can be made using standard recombinant DNA techniques. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in Robinson et al International Application No. PCT/US86/02269; Akira, et al European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison et al European Patent Application 173,494; Neuberger et al PCT International Publication No. WO 86/01533; Cabilly et al U.S. Patent No. 4,816,567; Cabilly et al European Patent Application 125,023; Better et al., Science 240: 1041-1043 (1988); Liu et al., Proc. Natl. Acad. Sci. USA 84: 3439-3443 (1987); Liu et al., J. Immunol. 139: 3521-3526 (1987); Sun et al., Proc. Natl. Acad. Sci. USA 84: 214-218 (1987); Nishimura et al., Canc. Res. 47: 999-1005 (1987); Wood et al., Nature 314: 446-449 (1985); and Shaw et al., J. Natl. Cancer Inst. 80: 1553-1559 (1988); Morrison, S. L., Science 229: 1202-1207 (1985); Oi et al., BioTechniques 4: 214 (1986); Winter U.S. Patent 5,225,539; Jones et al., Nature 321: 552-525 (1986); Verhoeyan et al., Science 239: 1534; and Beidler et al., J. Immunol. 141: 4053-4060 (1988).

[0132] Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced using transgenic mice that are incapable of expressing

endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. See, for example, Lonberg and Huszar, Int. Rev. Immunol. 13: 65-93 (1995); and U.S. Patent Nos. 5,625,126; 5,633,425; 5,569,825; 5,661,016; and 5,545,806. In addition, companies such as Abgenix, Inc. (Fremont, CA) and Medarex, Inc. (Princeton, NJ), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above. Completely human antibodies that recognize a selected epitope also can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody (e.g., a murine antibody) is used to guide the selection of a completely human antibody recognizing the same epitope. This technology is described for example by Jespers et al., Bio/Technology 12: 899-903 (1994).

[0133] An antibody can be a single chain antibody. A single chain antibody (scFV) can be engineered (see, e.g., Colcher et al., Ann. N Y Acad. Sci. 880: 263-80 (1999); and Reiter, Clin. Cancer Res. 2: 245-52 (1996)). Single chain antibodies can be dimerized or multimerized to generate multivalent antibodies having specificities for different epitopes of the same target polypeptide.

[0134] Antibodies also may be selected or modified so that they exhibit reduced or no ability to bind an Fc receptor. For example, an antibody may be an isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor (e.g., it has a mutagenized or deleted Fc receptor binding region).

[0135] Also, an antibody (or fragment thereof) may be conjugated to a therapeutic moiety such as a cytotoxin, a therapeutic agent or a radioactive metal ion. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1 dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thiotepa chlorambucil, melphalan, carmustine (BCNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

[0136] Antibody conjugates can be used for modifying a given biological response. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a polypeptide such as tumor necrosis factor, gamma-interferon, alpha-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator; or, biological response modifiers such as, for

example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors. Also, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, for example.

[0137] An antibody (e.g., monoclonal antibody) can be used to isolate target polypeptides by standard techniques, such as affinity chromatography or immunoprecipitation. Moreover, an antibody can be used to detect a target polypeptide (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the polypeptide. Antibodies can be used diagnostically to monitor polypeptide levels in tissue as part of a clinical testing procedure, e.g., to determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance (i.e., antibody labeling). Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, ß-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I, ^{131}I, ^{35}S or ^{3}H. Also, an antibody can be utilized as a test molecule for determining whether it can treat osteoarthritis, and as a therapeutic for administration to a subject for treating osteoarthritis.

[0138] An antibody can be made by immunizing with a purified antigen, or a fragment thereof, e.g., a fragment described herein, a membrane associated antigen, tissues, e.g., crude tissue preparations, whole cells, preferably living cells, lysed cells, or cell fractions.

[0139] Included herein are antibodies which bind only a native polypeptide, only denatured or otherwise non-native polypeptide, or which bind both, as well as those having linear or conformational epitopes. Conformational epitopes sometimes can be identified by selecting antibodies that bind to native but not denatured polypeptide. Also featured are antibodies that specifically bind to a polypeptide variant associated with osteoarthritis.

Methods for Identifying Candidate Therapeutics for Treating Osteoarthritis

[0140] Current therapies for the treatment of osteoarthritis have limited efficacy, limited tolerability and significant mechanism-based side effects, and few of the available therapies adequately address underlying defects. Current therapeutic approaches were largely developed in the absence of defined molecular targets or even a solid understanding of disease pathogenesis. Therefore, provided are

methods of identifying candidate therapeutics that target biochemical pathways related to the development of osteoarthritis.

[0141] Thus, featured herein are methods for identifying a candidate therapeutic for treating osteoarthritis. The methods comprise contacting a test molecule with a target molecule in a system. A "target molecule" as used herein refers to a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid, a substantially identical nucleic acid thereof, or a fragment thereof, and an encoded polypeptide of the foregoing. The methods also comprise determining the presence or absence of an interaction between the test molecule and the target molecule, where the presence of an interaction between the test molecule and the nucleic acid or polypeptide identifies the test molecule as a candidate osteoarthritis therapeutic. The interaction between the test molecule and the target molecule may be quantified.

[0142] Test molecules and candidate therapeutics include, but are not limited to, compounds, antisense nucleic acids, siRNA molecules, ribozymes, polypeptides or proteins encoded by a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleotide sequence, or a substantially identical sequence or fragment thereof, and immunotherapeutics (e.g., antibodies and HLA-presented polypeptide fragments). A test molecule or candidate therapeutic may act as a modulator of target molecule concentration or target molecule function in a system. A "modulator" may agonize (i.e., up-regulates) or antagonize (i.e., down-regulates) a target molecule concentration partially or completely in a system by affecting such cellular functions as DNA replication and/or DNA processing (e.g., DNA methylation or DNA repair), RNA transcription and/or RNA processing (e.g., removal of intronic sequences and/or translocation of spliced mRNA from the nucleus), polypeptide production (e.g., translation of the polypeptide from mRNA), and/or polypeptide post-translational modification (e.g., glycosylation, phosphorylation, and proteolysis of pro-polypeptides). A modulator may also agonize or antagonize a biological function of a target molecule partially or completely, where the function may include adopting a certain structural conformation, interacting with one or more binding partners, ligand binding, catalysis (e.g., phosphorylation, dephosphorylation, hydrolysis, methylation, and isomerization), and an effect upon a cellular event (*e.g.*, effecting progression of osteoarthritis).

[0143] As used herein, the term "system" refers to a cell free *in vitro* environment and a cell-based environment such as a collection of cells, a tissue, an organ, or an organism. A system is "contacted" with a test molecule in a variety of manners, including adding molecules in solution and allowing them to interact with one another by diffusion, cell injection, and any administration routes in an animal. As used herein, the term "interaction" refers to an effect of a test molecule on test molecule, where the effect sometimes is binding between the test molecule and the target molecule, and sometimes is an observable change in cells, tissue, or organism.

[0144] There are many standard methods for detecting the presence or absence of interaction between a test molecule and a target molecule. For example, titrametric, acidimetric, radiometric, NMR,

monolayer, polarographic, spectrophotometric, fluorescent, and ESR assays probative of a target molecule interaction may be utilized. Any modulator can be utilized in methods for detecting an interaction. For example, proteasome modulators (e.g., *PSMB1* includes a proteasome domain) are described in WO-2004014882 and Roesel et al. Proceedings of the American Association of Cancer Research 2003, 44:1st Ed (Abs 1769), and bortezomib (Velcade, MLN-341, LDP-341 and PS-341), a ubiquitin proteosome inhibitor, is used for the treatment of multiple myeloma.

[0145] Test molecule/target molecule interactions can be detected and/or quantified using assays known in the art. For example, an interaction can be determined by labeling the test molecule and/or the target molecule, where the label is covalently or non-covalently attached to the test molecule or target molecule. The label is sometimes a radioactive molecule such as ^{125}I, ^{131}I, ^{35}S or ^{3}H, which can be detected by direct counting of radioemission or by scintillation counting. Also, enzymatic labels such as horseradish peroxidase, alkaline phosphatase, or luciferase may be utilized where the enzymatic label can be detected by determining conversion of an appropriate substrate to product. In addition, presence or absence of an interaction can be determined without labeling. For example, a microphysiometer (*e.g.*, Cytosensor) is an analytical instrument that measures the rate at which a cell acidifies its environment using a light-addressable potentiometric sensor (LAPS). Changes in this acidification rate can be used as an indication of an interaction between a test molecule and target molecule (McConnell, H. M. *et al., Science 257:* 1906-1912 (1992)).

[0146] In cell-based systems, cells typically include a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid, an encoded polypeptide, or substantially identical nucleic acid or polypeptide thereof, and are often of mammalian origin, although the cell can be of any origin. Whole cells, cell homogenates, and cell fractions (*e.g.*, cell membrane fractions) can be subjected to analysis. Where interactions between a test molecule with a target polypeptide are monitored, soluble and/or membrane bound forms of the polypeptide may be utilized. Where membrane-bound forms of the polypeptide are used, it may be desirable to utilize a solubilizing agent. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)$_n$, 3-[(3-cholamidopropyl)dimethylamminio]-1-propane sulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylamminio]-2-hydroxy-1-propane sulfonate (CHAPSO), or N-dodecyl-N,N-dimethyl-3-ammonio-1-propane sulfonate.

[0147] An interaction between a test molecule and target molecule also can be detected by monitoring fluorescence energy transfer (FET) (*see, e.g.*, Lakowicz *et al.*, U.S. Patent No. 5,631,169; Stavrianopoulos *et al.* U.S. Patent No. 4,868,103). A fluorophore label on a first, "donor" molecule is selected such that its emitted fluorescent energy will be absorbed by a fluorescent label on a second,

"acceptor" molecule, which in turn is able to fluoresce due to the absorbed energy. Alternately, the "donor" polypeptide molecule may simply utilize the natural fluorescent energy of tryptophan residues. Labels are chosen that emit different wavelengths of light, such that the "acceptor" molecule label may be differentiated from that of the "donor". Since the efficiency of energy transfer between the labels is related to the distance separating the molecules, the spatial relationship between the molecules can be assessed. In a situation in which binding occurs between the molecules, the fluorescent emission of the "acceptor" molecule label in the assay should be maximal. An FET binding event can be conveniently measured through standard fluorometric detection means well known in the art (*e.g.*, using a fluorimeter).

[0148] In another embodiment, determining the presence or absence of an interaction between a test molecule and a target molecule can be effected by monitoring surface plasmon resonance (*see, e.g.*, Sjolander & Urbaniczk, *Anal. Chem. 63:* 2338-2345 (1991) and Szabo *et al., Curr. Opin. Struct. Biol. 5:* 699-705 (1995)). "Surface plasmon resonance" or "biomolecular interaction analysis (BIA)" can be utilized to detect biospecific interactions in real time, without labeling any of the interactants (*e.g.*, BIAcore). Changes in the mass at the binding surface (indicative of a binding event) result in alterations of the refractive index of light near the surface (the optical phenomenon of surface plasmon resonance (SPR)), resulting in a detectable signal which can be used as an indication of real-time reactions between biological molecules.

[0149] In another embodiment, the target molecule or test molecules are anchored to a solid phase, facilitating the detection of target molecule/test molecule complexes and separation of the complexes from free, uncomplexed molecules. The target molecule or test molecule is immobilized to the solid support. In an embodiment, the target molecule is anchored to a solid surface, and the test molecule, which is not anchored, can be labeled, either directly or indirectly, with detectable labels discussed herein.

[0150] It may be desirable to immobilize a target molecule, an anti-target molecule antibody, and/or test molecules to facilitate separation of target molecule/test molecule complexes from uncomplexed forms, as well as to accommodate automation of the assay. The attachment between a test molecule and/or target molecule and the solid support may be covalent or non-covalent (*see, e.g.*, U.S. Patent No. 6,022,688 for non-covalent attachments). The solid support may be one or more surfaces of the system, such as one or more surfaces in each well of a microtiter plate, a surface of a silicon wafer, a surface of a bead (*see, e.g.*, Lam, *Nature 354:* 82-84 (1991)) that is optionally linked to another solid support, or a channel in a microfluidic device, for example. Types of solid supports, linker molecules for covalent and non-covalent attachments to solid supports, and methods for immobilizing nucleic acids and other molecules to solid supports are well known (*see, e.g.*, U.S. Patent Nos. 6,261,776; 5,900,481; 6,133,436; and 6,022,688; and WIPO publication WO 01/18234).

[0151] In an embodiment, target molecule may be immobilized to surfaces via biotin and streptavidin. For example, biotinylated target polypeptide can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, IL), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). In another embodiment, a target polypeptide can be prepared as a fusion polypeptide. For example, glutathione-S-transferase/target polypeptide fusion can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivitized microtiter plates, which are then combined with a test molecule under conditions conducive to complex formation (*e.g.*, at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components, or the matrix is immobilized in the case of beads, and complex formation is determined directly or indirectly as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of target molecule binding or activity is determined using standard techniques.

[0152] In an embodiment, the non-immobilized component is added to the coated surface containing the anchored component. After the reaction is complete, unreacted components are removed (*e.g.*, by washing) under conditions such that a significant percentage of complexes formed will remain immobilized to the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of manners. Where the previously non-immobilized component is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the previously non-immobilized component is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface, *e.g.*, by adding a labeled antibody specific for the immobilized component, where the antibody, in turn, can be directly labeled or indirectly labeled with, *e.g.*, a labeled anti-Ig antibody.

[0153] In another embodiment, an assay is performed utilizing antibodies that specifically bind target molecule or test molecule but do not interfere with binding of the target molecule to the test molecule. Such antibodies can be derivitized to a solid support, and unbound target molecule may be immobilized by antibody conjugation. Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the target molecule, as well as enzyme-linked assays which rely on detecting an enzymatic activity associated with the target molecule.

[0154] Cell free assays also can be conducted in a liquid phase. In such an assay, reaction products are separated from unreacted components, by any of a number of standard techniques, including but not limited to: differential centrifugation (*see, e.g.*, Rivas, G., and Minton, *Trends Biochem Sci Aug;18(8):* 284-7 (1993)); chromatography (gel filtration chromatography, ion-exchange chromatography); electrophoresis (*see, e.g.*, Ausubel *et al., eds. Current Protocols in Molecular Biology , J. Wiley:* New York (1999)); and immunoprecipitation (*see, e.g.*, Ausubel *et al., eds., supra*). Media and

chromatographic techniques are known to one skilled in the art (*see, e.g.*, Heegaard, *J Mol. Recognit. Winter; 11(1-6):* 141-8 (1998); Hage & Tweed, *J. Chromatogr. B Biomed. Sci. Appl. Oct 10; 699 (1-2): 499-525* (1997)). Further, fluorescence energy transfer may also be conveniently utilized, as described herein, to detect binding without further purification of the complex from solution.

[0155] In another embodiment, modulators of target molecule expression are identified. For example, a cell or cell free mixture is contacted with a candidate compound and the expression of target mRNA or target polypeptide is evaluated relative to the level of expression of target mRNA or target polypeptide in the absence of the candidate compound. When expression of target mRNA or target polypeptide is greater in the presence of the candidate compound than in its absence, the candidate compound is identified as an agonist of target mRNA or target polypeptide expression. Alternatively, when expression of target mRNA or target polypeptide is less (*e.g.*, less with statistical significance) in the presence of the candidate compound than in its absence, the candidate compound is identified as an antagonist or inhibitor of target mRNA or target polypeptide expression. The level of target mRNA or target polypeptide expression can be determined by methods described herein.

[0156] In another embodiment, binding partners that interact with a target molecule are detected. The target molecules can interact with one or more cellular or extracellular macromolecules, such as polypeptides *in vivo*, and these interacting molecules are referred to herein as "binding partners." Binding partners can agonize or antagonize target molecule biological activity. Also, test molecules that agonize or antagonize interactions between target molecules and binding partners can be useful as therapeutic molecules as they can up-regulate or down-regulated target molecule activity *in vivo* and thereby treat osteoarthritis.

[0157] Binding partners of target molecules can be identified by methods known in the art. For example, binding partners may be identified by lysing cells and analyzing cell lysates by electrophoretic techniques. Alternatively, a two-hybrid assay or three-hybrid assay can be utilized (*see, e.g.*, U.S. Patent No. 5,283,317; Zervos *et al., Cell 72:223-232* (1993); Madura *et al., J. Biol. Chem. 268:* 12046-12054 (1993); Bartel *et al., Biotechniques 14:* 920-924 (1993); Iwabuchi *et al., Oncogene 8:* 1693-1696 (1993); and Brent WO94/10300). A two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. The assay often utilizes two different DNA constructs. In one construct, a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid (sometimes referred to as the "bait") is fused to a gene encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In another construct, a DNA sequence from a library of DNA sequences that encodes a potential binding partner (sometimes referred to as the "prey") is fused to a gene that encodes an activation domain of the known transcription factor. Sometimes, a *PSMB1, TBP, PDCD2, ELP3, CHDC1* or *ERG* nucleic acid can be fused to the activation domain. If the "bait" and the "prey" molecules interact *in vivo*, the DNA-binding and activation domains of the transcription factor are

brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to identify the potential binding partner.

[0158] In an embodiment for identifying test molecules that antagonize or agonize complex formation between target molecules and binding partners, a reaction mixture containing the target molecule and the binding partner is prepared, under conditions and for a time sufficient to allow complex formation. The reaction mixture often is provided in the presence or absence of the test molecule. The test molecule can be included initially in the reaction mixture, or can be added at a time subsequent to the addition of the target molecule and its binding partner. Control reaction mixtures are incubated without the test molecule or with a placebo. Formation of any complexes between the target molecule and the binding partner then is detected. Decreased formation of a complex in the reaction mixture containing test molecule as compared to in a control reaction mixture indicates that the molecule antagonizes target molecule/binding partner complex formation. Alternatively, increased formation of a complex in the reaction mixture containing test molecule as compared to in a control reaction mixture indicates that the molecule agonizes target molecule/binding partner complex formation. In another embodiment, complex formation of target molecule/binding partner can be compared to complex formation of mutant target molecule/binding partner (*e.g.*, amino acid modifications in a target polypeptide). Such a comparison can be important in those cases where it is desirable to identify test molecules that modulate interactions of mutant but not non-mutated target gene products.

[0159] The assays can be conducted in a heterogeneous or homogeneous format. In heterogeneous assays, target molecule and/or the binding partner are immobilized to a solid phase, and complexes are detected on the solid phase at the end of the reaction. In homogeneous assays, the entire reaction is carried out in a liquid phase. In either approach, the order of addition of reactants can be varied to obtain different information about the molecules being tested. For example, test compounds that agonize target molecule/binding partner interactions can be identified by conducting the reaction in the presence of the test molecule in a competition format. Alternatively, test molecules that agonize preformed complexes, *e.g.*, molecules with higher binding constants that displace one of the components from the complex, can be tested by adding the test compound to the reaction mixture after complexes have been formed.

[0160] In a heterogeneous assay embodiment, the target molecule or the binding partner is anchored onto a solid surface (*e.g.*, a microtiter plate), while the non-anchored species is labeled, either directly or indirectly. The anchored molecule can be immobilized by non-covalent or covalent attachments. Alternatively, an immobilized antibody specific for the molecule to be anchored can be used to anchor the molecule to the solid surface. The partner of the immobilized species is exposed to the coated surface with or without the test molecule. After the reaction is complete, unreacted components are removed

(*e.g.*, by washing) such that a significant portion of any complexes formed will remain immobilized on the solid surface. Where the non-immobilized species is pre-labeled, the detection of label immobilized on the surface is indicative of complex. Where the non-immobilized species is not pre-labeled, an indirect label can be used to detect complexes anchored to the surface; *e.g.*, by using a labeled antibody specific for the initially non-immobilized species. Depending upon the order of addition of reaction components, test compounds that inhibit complex formation or that disrupt preformed complexes can be detected.

[0161] In another embodiment, the reaction can be conducted in a liquid phase in the presence or absence of test molecule, where the reaction products are separated from unreacted components, and the complexes are detected (*e.g.*, using an immobilized antibody specific for one of the binding components to anchor any complexes formed in solution, and a labeled antibody specific for the other partner to detect anchored complexes). Again, depending upon the order of addition of reactants to the liquid phase, test compounds that inhibit complex or that disrupt preformed complexes can be identified.

[0162] In an alternate embodiment, a homogeneous assay can be utilized. For example, a preformed complex of the target gene product and the interactive cellular or extracellular binding partner product is prepared. One or both of the target molecule or binding partner is labeled, and the signal generated by the label(s) is quenched upon complex formation (*e.g.*, U.S. Patent No. 4,109,496 that utilizes this approach for immunoassays). Addition of a test molecule that competes with and displaces one of the species from the preformed complex will result in the generation of a signal above background. In this way, test substances that disrupt target molecule/binding partner complexes can be identified.

[0163] Candidate therapeutics for treating osteoarthritis are identified from a group of test molecules that interact with a target molecule. Test molecules are normally ranked according to the degree with which they modulate (*e.g.*, agonize or antagonize) a function associated with the target molecule (*e.g.*, DNA replication and/or processing, RNA transcription and/or processing, polypeptide production and/or processing, and/or biological function/activity), and then top ranking modulators are selected. Also, pharmacogenomic information described herein can determine the rank of a modulator. The top 10% of ranked test molecules often are selected for further testing as candidate therapeutics, and sometimes the top 15%, 20%, or 25% of ranked test molecules are selected for further testing as candidate therapeutics. Candidate therapeutics typically are formulated for administration to a subject.

Therapeutic Formulations

[0164] Formulations and pharmaceutical compositions typically include in combination with a pharmaceutically acceptable carrier one or more target molecule modulators. The modulator often is a test molecule identified as having an interaction with a target molecule by a screening method described above. The modulator may be a compound, an antisense nucleic acid, a ribozyme, an antibody, or a

binding partner. Also, formulations may comprise a target polypeptide or fragment thereof in combination with a pharmaceutically acceptable carrier.

[0165] As used herein, the term "pharmaceutically acceptable carrier" includes solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Supplementary active compounds can also be incorporated into the compositions. Pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

[0166] A pharmaceutical composition typically is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerin, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

[0167] Oral compositions generally include an inert diluent or an edible carrier. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules, *e.g.*, gelatin capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

[0168] Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can

be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[0169] Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

[0170] For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

[0171] Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art. Molecules can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

[0172] In one embodiment, active molecules are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. Materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to

viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

[0173] It is advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier.

[0174] Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.,* for determining the LD_{50} (the dose lethal to 50% of the population) and the ED_{50} (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD_{50}/ED_{50}. Molecules which exhibit high therapeutic indices are preferred. While molecules that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

[0175] The data obtained from the cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such molecules lies preferably within a range of circulating concentrations that include the ED_{50} with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any molecules used in the methods described herein, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC_{50} (*i.e.*, the concentration of the test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

[0176] As defined herein, a therapeutically effective amount of protein or polypeptide (*i.e.*, an effective dosage) ranges from about 0.001 to 30 mg/kg body weight, sometimes about 0.01 to 25 mg/kg body weight, often about 0.1 to 20 mg/kg body weight, and more often about 1 to 10 mg/kg, 2 to 9 mg/kg, 3 to 8 mg/kg, 4 to 7 mg/kg, or 5 to 6 mg/kg body weight. The protein or polypeptide can be administered one time per week for between about 1 to 10 weeks, sometimes between 2 to 8 weeks, often between about 3 to 7 weeks, and more often for about 4, 5, or 6 weeks. The skilled artisan will appreciate that certain factors may influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a

therapeutically effective amount of a protein, polypeptide, or antibody can include a single treatment or, preferably, can include a series of treatments.

[0177] With regard to polypeptide formulations, featured herein is a method for treating osteoarthritis in a subject, which comprises contacting one or more cells in the subject with a first polypeptide, where the subject comprises a second polypeptide having one or more polymorphic variations associated with cancer, and where the first polypeptide comprises fewer polymorphic variations associated with cancer than the second polypeptide. The first and second polypeptides are encoded by a nucleic acid which comprises a nucleotide sequence in SEQ ID NO: 1-12; a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence encoded by a nucleotide sequence referenced in SEQ ID NO: 1-12; a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1-12 and a nucleotide sequence 90% or more identical to a nucleotide sequence in SEQ ID NO: 1-12. The subject often is a human.

[0178] For antibodies, a dosage of 0.1 mg/kg of body weight (generally 10 mg/kg to 20 mg/kg) is often utilized. If the antibody is to act in the brain, a dosage of 50 mg/kg to 100 mg/kg is often appropriate. Generally, partially human antibodies and fully human antibodies have a longer half-life within the human body than other antibodies. Accordingly, lower dosages and less frequent administration is often possible. Modifications such as lipidation can be used to stabilize antibodies and to enhance uptake and tissue penetration (*e.g.*, into the brain). A method for lipidation of antibodies is described by Cruikshank *et al., J. Acquired Immune Deficiency Syndromes and Human Retrovirology 14:*193 (1997).

[0179] Antibody conjugates can be used for modifying a given biological response, the drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a polypeptide such as tumor necrosis factor, alpha-interferon, beta-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors. Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980.

[0180] For compounds, exemplary doses include milligram or microgram amounts of the compound per kilogram of subject or sample weight, for example, about 1 microgram per kilogram to about 500 milligrams per kilogram, about 100 micrograms per kilogram to about 5 milligrams per kilogram, or about 1 microgram per kilogram to about 50 micrograms per kilogram. It is understood that appropriate

doses of a small molecule depend upon the potency of the small molecule with respect to the expression or activity to be modulated. When one or more of these small molecules is to be administered to an animal (*e.g.*, a human) in order to modulate expression or activity of a polypeptide or nucleic acid described herein, a physician, veterinarian, or researcher may, for example, prescribe a relatively low dose at first, subsequently increasing the dose until an appropriate response is obtained. In addition, it is understood that the specific dose level for any particular animal subject will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, gender, and diet of the subject, the time of administration, the route of administration, the rate of excretion, any drug combination, and the degree of expression or activity to be modulated.

[0181] With regard to nucleic acid formulations, gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (*see, e.g.,* U.S. Patent 5,328,470) or by stereotactic injection (*see e.g.*, Chen *et al.,* (1994) *Proc. Natl. Acad. Sci. USA 91*:3054-3057). Pharmaceutical preparations of gene therapy vectors can include a gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells (*e.g.*, retroviral vectors) the pharmaceutical preparation can include one or more cells which produce the gene delivery system. Examples of gene delivery vectors are described herein.

Therapeutic Methods

[0182] A therapeutic formulation described above can be administered to a subject in need of a therapeutic for inducing a desired biological response. Therapeutic formulations can be administered by any of the paths described herein. With regard to both prophylactic and therapeutic methods of treatment, such treatments may be specifically tailored or modified, based on knowledge obtained from pharmacogenomic analyses described herein.

[0183] As used herein, the term "treatment" is defined as the application or administration of a therapeutic formulation to a subject, or application or administration of a therapeutic agent to an isolated tissue or cell line from a subject with the purpose to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve or affect osteoarthritis, symptoms of osteoarthritis or a predisposition towards osteoarthritis. A therapeutic formulation includes, but is not limited to, small molecules, peptides, antibodies, ribozymes and antisense oligonucleotides. Administration of a therapeutic formulation can occur prior to the manifestation of symptoms characteristic of osteoarthritis, such that osteoarthritis is prevented or delayed in its progression. The appropriate therapeutic composition can be determined based on screening assays described herein.

[0184] As discussed, successful treatment of osteoarthritis can be brought about by techniques that serve to agonize target molecule expression or function, or alternatively, antagonize target molecule

expression or function. These techniques include administration of modulators that include, but are not limited to, small organic or inorganic molecules; antibodies (including, for example, polyclonal, monoclonal, humanized, anti-idiotypic, chimeric or single chain antibodies, and Fab, F(ab')$_2$ and Fab expression library fragments, scFV molecules, and epitope-binding fragments thereof); and peptides, phosphopeptides, or polypeptides.

[0185] Further, antisense and ribozyme molecules that inhibit expression of the target gene can also be used to reduce the level of target gene expression, thus effectively reducing the level of target gene activity. Still further, triple helix molecules can be utilized in reducing the level of target gene activity. Antisense, ribozyme and triple helix molecules are discussed above. It is possible that the use of antisense, ribozyme, and/or triple helix molecules to reduce or inhibit mutant gene expression can also reduce or inhibit the transcription (triple helix) and/or translation (antisense, ribozyme) of mRNA produced by normal target gene alleles, such that the concentration of normal target gene product present can be lower than is necessary for a normal phenotype. In such cases, nucleic acid molecules that encode and express target gene polypeptides exhibiting normal target gene activity can be introduced into cells via gene therapy method. Alternatively, in instances in that the target gene encodes an extracellular polypeptide, it can be preferable to co-administer normal target gene polypeptide into the cell or tissue in order to maintain the requisite level of cellular or tissue target gene activity.

[0186] Another method by which nucleic acid molecules may be utilized in treating or preventing osteoarthritis is use of aptamer molecules specific for target molecules. Aptamers are nucleic acid molecules having a tertiary structure which permits them to specifically bind to ligands (*see, e.g.*, Osborne, *et al., Curr. Opin. Chem. Biol.1(1):* 5-9 (1997); and Patel, D. J., *Curr. Opin. Chem. Biol. Jun;1(1):* 32-46 (1997)).

[0187] Yet another method of utilizing nucleic acid molecules for osteoarthritis treatment is gene therapy, which can also be referred to as allele therapy. Provided herein is a gene therapy method for treating osteoarthritis in a subject, which comprises contacting one or more cells in the subject or from the subject with a nucleic acid having a first nucleotide sequence (e.g., the first nucleotide sequence is identical to or substantially identical to a nucleotide sequence of SEQ ID NO: 1-12). Genomic DNA in the subject comprises a second nucleotide sequence having one or more polymorphic variations associated with osteoarthritis (e.g., the second nucleotide sequence is identical to or substantially identical to a nucleotide sequence of SEQ ID NO: 1-4). The first and second nucleotide sequences typically are substantially identical to one another, and the first nucleotide sequence comprises fewer polymorphic variations associated with osteoarthritis than the second nucleotide sequence. The first nucleotide sequence may comprise a gene sequence that encodes a full-length polypeptide or a fragment thereof. The subject is often a human. Allele therapy methods often are utilized in conjunction with a

method of first determining whether a subject has genomic DNA that includes polymorphic variants associated with osteoarthritis.

[0188] In another allele therapy embodiment, provided herein is a method which comprises contacting one or more cells in the subject or from the subject with a polypeptide encoded by a nucleic acid having a first nucleotide sequence (e.g., the first nucleotide sequence is identical to or substantially identical to the nucleotide sequence of SEQ ID NO: 1-12). Genomic DNA in the subject comprises a second nucleotide sequence having one or more polymorphic variations associated with osteoarthritis (e.g., the second nucleotide sequence is identical to or substantially identical to a nucleotide sequence of SEQ ID NO: 1-4). The first and second nucleotide sequences typically are substantially identical to one another, and the first nucleotide sequence comprises fewer polymorphic variations associated with osteoarthritis than the second nucleotide sequence. The first nucleotide sequence may comprise a gene sequence that encodes a full-length polypeptide or a fragment thereof. The subject is often a human.

[0189] For antibody-based therapies, antibodies can be generated that are both specific for target molecules and that reduce target molecule activity. Such antibodies may be administered in instances where antagonizing a target molecule function is appropriate for the treatment of osteoarthritis.

[0190] In circumstances where stimulating antibody production in an animal or a human subject by injection with a target molecule is harmful to the subject, it is possible to generate an immune response against the target molecule by use of anti-idiotypic antibodies (*see, e.g.*, Herlyn, *Ann. Med.;31(1):* 66-78 (1999); and Bhattacharya-Chatterjee & Foon, *Cancer Treat. Res.; 94:* 51-68 (1998)). Introducing an anti-idiotypic antibody to a mammal or human subject often stimulates production of anti-anti-idiotypic antibodies, which typically are specific to the target molecule. Vaccines directed to osteoarthritis also may be generated in this fashion.

[0191] In instances where the target molecule is intracellular and whole antibodies are used, internalizing antibodies may be preferred. Lipofectin or liposomes can be used to deliver the antibody or a fragment of the Fab region that binds to the target antigen into cells. Where fragments of the antibody are used, the smallest inhibitory fragment that binds to the target antigen is preferred. For example, peptides having an amino acid sequence corresponding to the Fv region of the antibody can be used. Alternatively, single chain neutralizing antibodies that bind to intracellular target antigens can also be administered. Such single chain antibodies can be administered, for example, by expressing nucleotide sequences encoding single-chain antibodies within the target cell population (*see, e.g.*, Marasco *et al., Proc. Natl. Acad. Sci. USA 90:* 7889-7893 (1993)).

[0192] Modulators can be administered to a patient at therapeutically effective doses to treat osteoarthritis. A therapeutically effective dose refers to an amount of the modulator sufficient to result in amelioration of symptoms of osteoarthritis. Toxicity and therapeutic efficacy of modulators can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, for

determining the LD_{50} (the dose lethal to 50% of the population) and the ED_{50} (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD_{50}/ED_{50}. Modulators that exhibit large therapeutic indices are preferred. While modulators that exhibit toxic side effects can be used, care should be taken to design a delivery system that targets such molecules to the site of affected tissue in order to minimize potential damage to uninfected cells, thereby reducing side effects.

[0193] Data obtained from cell culture assays and animal studies can be used in formulating a range of dosages for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED_{50} with little or no toxicity. The dosage can vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the methods described herein, the therapeutically effective dose can be estimated initially from cell culture assays. A dose can be formulated in animal models to achieve a circulating plasma concentration range that includes the IC_{50} (*i.e.*, the concentration of the test compound that achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma can be measured, for example, by high performance liquid chromatography.

[0194] Another example of effective dose determination for an individual is the ability to directly assay levels of "free" and "bound" compound in the serum of the test subject. Such assays may utilize antibody mimics and/or "biosensors" that have been created through molecular imprinting techniques. Molecules that modulate target molecule activity are used as a template, or "imprinting molecule", to spatially organize polymerizable monomers prior to their polymerization with catalytic reagents. The subsequent removal of the imprinted molecule leaves a polymer matrix which contains a repeated "negative image" of the compound and is able to selectively rebind the molecule under biological assay conditions. A detailed review of this technique can be seen in Ansell *et al., Current Opinion in Biotechnology 7:* 89-94 (1996) and in Shea, *Trends in Polymer Science 2:* 166-173 (1994). Such "imprinted" affinity matrixes are amenable to ligand-binding assays, whereby the immobilized monoclonal antibody component is replaced by an appropriately imprinted matrix. An example of the use of such matrixes in this way can be seen in Vlatakis, *et al., Nature 361:* 645-647 (1993). Through the use of isotope-labeling, the "free" concentration of compound which modulates target molecule expression or activity readily can be monitored and used in calculations of IC_{50}. Such "imprinted" affinity matrixes can also be designed to include fluorescent groups whose photon-emitting properties measurably change upon local and selective binding of target compound. These changes readily can be assayed in real time using appropriate fiberoptic devices, in turn allowing the dose in a test subject to be quickly optimized based on its individual IC_{50}. An example of such a "biosensor" is discussed in Kriz *et al., Analytical Chemistry 67:* 2142-2144 (1995).

[0195] The examples set forth below are intended to illustrate but not limit the invention.

Examples

[0196] In the following studies a group of subjects was selected according to specific parameters relating to osteoarthritis. Nucleic acid samples obtained from individuals in the study group were subjected to genetic analysis, which identified associations between osteoarthritis and polymorphisms in the following genes or regions: *chromosome 6 (6q27), ELP3, CHDC1*, and *ERG* (herein referred to as "targets"). The polymorphisms were genotyped again in two replication cohorts consisting of individuals selected for OA. In addition, SNPs proximal to the incident polymorphisms were identified and allelotyped in OA case and control pools. Methods are described for producing *PSMB1, TBP, PDCD2, ELP3, CHDC1*, and *ERG* polypeptide and polypeptide variants thereof *in vitro* or *in vivo; PSMB1, TBP, PDCD2, ELP3, CHDC1*, and *ERG* nucleic acids or polypeptides and variants thereof are utilized for screening test molecules for those that interact with *PSMB1, TBP, PDCD2, ELP3, CHDC1*, and *ERG* molecules. Test molecules identified as interactors with *PSMB1, TBP, PDCD2, ELP3, CHDC1*, and *ERG* molecules and variants thereof are further screened *in vivo* to determine whether they treat osteoarthritis.

Example 1

Samples and Pooling Strategies

Sample Selection

[0197] Blood samples were collected from individuals diagnosed with knee osteoarthritis, which were referred to as case samples. Also, blood samples were collected from individuals not diagnosed with knee osteoarthritis as gender and age-matched controls. A database was created that listed all phenotypic trait information gathered from individuals for each case and control sample. Genomic DNA was extracted from each of the blood samples for genetic analyses.

DNA Extraction from Blood Samples

[0198] Six to ten milliliters of whole blood was transferred to a 50 ml tube containing 27 ml of red cell lysis solution (RCL). The tube was inverted until the contents were mixed. Each tube was incubated for 10 minutes at room temperature and inverted once during the incubation. The tubes were then centrifuged for 20 minutes at 3000 x g and the supernatant was carefully poured off. 100-200 µl of residual liquid was left in the tube and was pipetted repeatedly to resuspend the pellet in the residual supernatant. White cell lysis solution (WCL) was added to the tube and pipetted repeatedly until completely mixed. While no incubation was normally required, the solution was incubated at 37°C or

room temperature if cell clumps were visible after mixing until the solution was homogeneous. 2 ml of protein precipitation was added to the cell lysate. The mixtures were vortexed vigorously at high speed for 20 sec to mix the protein precipitation solution uniformly with the cell lysate, and then centrifuged for 10 minutes at 3000 x g. The supernatant containing the DNA was then poured into a clean 15 ml tube, which contained 7 ml of 100% isopropanol. The samples were mixed by inverting the tubes gently until white threads of DNA were visible. Samples were centrifuged for 3 minutes at 2000 x g and the DNA was visible as a small white pellet. The supernatant was decanted and 5 ml of 70% ethanol was added to each tube. Each tube was inverted several times to wash the DNA pellet, and then centrifuged for 1 minute at 2000 x g. The ethanol was decanted and each tube was drained on clean absorbent paper. The DNA was dried in the tube by inversion for 10 minutes, and then 1000 µl of 1X TE was added. The size of each sample was estimated, and less TE buffer was added during the following DNA hydration step if the sample was smaller. The DNA was allowed to rehydrate overnight at room temperature, and DNA samples were stored at 2-8°C.

[0199] DNA was quantified by placing samples on a hematology mixer for at least 1 hour. DNA was serially diluted (typically 1:80, 1:160, 1:320, and 1:640 dilutions) so that it would be within the measurable range of standards. 125 µl of diluted DNA was transferred to a clear U-bottom microtitre plate, and 125 µl of 1X TE buffer was transferred into each well using a multichannel pipette. The DNA and 1X TE were mixed by repeated pipetting at least 15 times, and then the plates were sealed. 50 µl of diluted DNA was added to wells A5-H12 of a black flat bottom microtitre plate. Standards were inverted six times to mix them, and then 50 µl of 1X TE buffer was pipetted into well A1, 1000 ng/ml of standard was pipetted into well A2, 500 ng/ml of standard was pipetted into well A3, and 250 ng/ml of standard was pipetted into well A4. PicoGreen (Molecular Probes, Eugene, Oregon) was thawed and freshly diluted 1:200 according to the number of plates that were being measured. PicoGreen was vortexed and then 50µl was pipetted into all wells of the black plate with the diluted DNA. DNA and PicoGreen were mixed by pipetting repeatedly at least 10 times with the multichannel pipette. The plate was placed into a Fluoroskan Ascent Machine (microplate fluorometer produced by Labsystems) and the samples were allowed to incubate for 3 minutes before the machine was run using filter pairs 485 nm excitation and 538 nm emission wavelengths. Samples having measured DNA concentrations of greater than 450 ng/µl were re-measured for conformation. Samples having measured DNA concentrations of 20 ng/µl or less were re-measured for confirmation.

Pooling Strategies – Discovery Cohort

[0200] Samples were derived from the Nottingham knee OA family study (UK) where index cases were identified through a knee replacement registry. Siblings were approached and assessed with knee x-

rays and assigned status as affected or unaffected. In all 1,157 individuals were available. In order to create same-sex pools of appropriate sizes, 335 unrelated female individuals with OA from the Nottingham OA sample were selected for the case pool. The control pool was made up of unrelated female individuals from the St. Thomas twin study (England) with normal knee x-rays and without other indications of OA, regardless of anatomical location, as well as lacking family history of OA. The St. Thomas twin study consists of Caucasian, female participants from the St. Thomas' Hospital, London, adult-twin registry, which is a voluntary registry of >4,000 twin pairs ranging from 18 to 76 years of age. The female case samples and female control samples are described further in Table 1 below.

[0201] A select set of samples from each group were utilized to generate pools, and one pool was created for each group. Each individual sample in a pool was represented by an equal amount of genomic DNA. For example, where 25 ng of genomic DNA was utilized in each PCR reaction and there were 200 individuals in each pool, each individual would provide 125 pg of genomic DNA. Inclusion or exclusion of samples for a pool was based upon the following criteria: the sample was derived from an individual characterized as Caucasian; the sample was derived from an individual of British paternal and maternal descent; case samples were derived from individuals diagnosed with specific knee osteoarthritis (OA) and were recruited from an OA knee replacement clinic. Control samples were derived from individuals free of OA, family history of OA, and rheumatoid arthritis. Also, sufficient genomic DNA was extracted from each blood sample for all allelotyping and genotyping reactions performed during the study. Phenotype information from each individual was collected and included age of the individual, gender, family history of OA, general medical information (e.g., height, weight, thyroid disease, diabetes, psoriasis, hysterectomy), joint history (previous and current symptoms, joint-related operations, age at onset of symptoms, date of primary diagnosis, age of individual as of primary diagnosis and order of involvement), and knee-related findings (crepitus, restricted passive movement, bony swelling/deformity). Additional knee information included knee history, current symptoms, any major knee injury, menisectomy, knee replacement surgery, age of surgery, and treatment history (including hormone replace therapy (HRT)). Samples that met these criteria were added to appropriate pools based on disease status.

[0202] The selection process yielded the pools set forth in Table 1, which were used in the studies that follow:

TABLE 1

	Female case	**Female control**
Pool size (Number)	335	335
Pool Criteria (ex: case/control)	control	case

Mean Age (ex: years)	57.21	69.95

Example 2

Association of Polymorphic Variants with Osteoarthritis

[0203] A whole-genome screen was performed to identify particular SNPs associated with occurrence of osteoarthritis. As described in Example 1, two sets of samples were utilized, which included samples from female individuals having knee osteoarthritis (osteoarthritis cases), and samples from female individuals not having knee osteoarthritis (female controls). The initial screen of each pool was performed in an allelotyping study, in which certain samples in each group were pooled. By pooling DNA from each group, an allele frequency for each SNP in each group was calculated. These allele frequencies were then compared to one another. Particular SNPs were considered as being associated with osteoarthritis when allele frequency differences calculated between case and control pools were statistically significant. SNP disease association results obtained from the allelotyping study were then validated by genotyping each associated SNP across all samples from each pool. The results of the genotyping then were analyzed, allele frequencies for each group were calculated from the individual genotyping results, and a p-value was calculated to determine whether the case and control groups had statistically significant differences in allele frequencies for a particular SNP. When the genotyping results agreed with the original allelotyping results, the SNP disease association was considered validated at the genetic level.

SNP Panel Used for Genetic Analyses

[0204] A whole-genome SNP screen began with an initial screen of approximately 25,000 SNPs over each set of disease and control samples using a pooling approach. The pools studied in the screen are described in Example 1. The SNPs analyzed in this study were part of a set of 25,488 SNPs confirmed as being statistically polymorphic as each is characterized as having a minor allele frequency of greater than 10%. The SNPs in the set reside in genes or in close proximity to genes, and many reside in gene exons. Specifically, SNPs in the set are located in exons, introns, and within 5,000 base-pairs upstream of a transcription start site of a gene. In addition, SNPs were selected according to the following criteria: they are located in ESTs; they are located in Locuslink or Ensembl genes; and they are located in Genomatix promoter predictions. SNPs in the set were also selected on the basis of even spacing across the genome, as depicted in Table 2.

[0205] A case-control study design using a whole genome association strategy involving approximately 28,000 single nucleotide polymorphisms (SNPs) was employed. Approximately 25,000

SNPs were evenly spaced in gene-based regions of the human genome with a median inter-marker distance of about 40,000 base pairs. Additionally, approximately 3,000 SNPs causing amino acid substitutions in genes described in the literature as candidates for various diseases were used. The case-control study samples were of female Caucasian origin (British paternal and maternal descent) 670 individuals were equally distributed in two groups: female controls and female cases. The whole genome association approach was first conducted on 2 DNA pools representing the 2 groups. Significant markers were confirmed by individual genotyping.

TABLE 2

General Statistics		Spacing Statistics	
Total # of SNPs	25,488	Median	37,058 bp
# of Exonic SNPs	>4,335 (17%)	Minimum*	1,000 bp
# SNPs with refSNP ID	20,776 (81%)	Maximum*	3,000,000 bp
Gene Coverage	>10,000	Mean	122,412 bp
Chromosome Coverage	All	Std Deviation	373,325 bp
		Excludes outliers	

Allelotyping and Genotyping Results

[0206] The genetic studies summarized above and described in more detail below identified allelic variants in the target genes that are associated with osteoarthritis.

Assay for Verifying, Allelotyping, and Genotyping SNPs

[0207] A MassARRAY™ system (Sequenom, Inc.) was utilized to perform SNP genotyping in a high-throughput fashion. This genotyping platform was complemented by a homogeneous, single-tube assay method (hME™ or homogeneous MassEXTEND™ (Sequenom, Inc.)) in which two genotyping primers anneal to and amplify a genomic target surrounding a polymorphic site of interest. A third primer (the MassEXTEND™ primer), which is complementary to the amplified target up to but not including the polymorphism, was then enzymatically extended one or a few bases through the polymorphic site and then terminated.

[0208] For each polymorphism, SpectroDESIGNER™ software (Sequenom, Inc.) was used to generate a set of PCR primers and a MassEXTEND™ primer which where used to genotype the polymorphism. Other primer design software could be used or one of ordinary skill in the art could manually design primers based on his or her knowledge of the relevant factors and considerations in designing such primers. Table 3 shows PCR primers and Table 4 shows extension primers used for analyzing polymorphisms. The initial PCR amplification reaction was performed in a 5 μl total volume containing 1X PCR buffer with 1.5 mM $MgCl_2$ (Qiagen), 200 μM each of dATP, dGTP, dCTP, dTTP

(Gibco-BRL), 2.5 ng of genomic DNA, 0.1 units of HotStar DNA polymerase (Qiagen), and 200 nM each of forward and reverse PCR primers specific for the polymorphic region of interest.

TABLE 3: PCR Primers

SNP Reference	Forward PCR primer	Reverse PCR primer
rs756519	ACGTTGGATGTCTAGAGACACCTGAGGTTG	ACGTTGGATGTGTTTCACTTCAGAGCCCTG
rs1042327	ACGTTGGATGAACTTCACATCACAGCTCCC	ACGTTGGATGCAGAAGTTGGGTTTTCCAGC
rs8770	ACGTTGGATGCTGTCACTGGACACTTTTG	ACGTTGGATGAAAATAGAGGTGCAGAGATG
rs1563055	ACGTTGGATGAGTTCTTTCTCCTCACATTG	ACGTTGGATGCCCTTTAGAAGCACATACTC
rs912428	ACGTTGGATGACTACATCCATTCCAGGGAG	ACGTTGGATGTCAGATCAGAGTGAGTTTAG
rs1888475	ACGTTGGATGACCCCTGGCAAGTGAATTAC	ACGTTGGATGGGGAGGTGGATGTTCTTATC

[0209] Samples were incubated at 95°C for 15 minutes, followed by 45 cycles of 95°C for 20 seconds, 56°C for 30 seconds, and 72°C for 1 minute, finishing with a 3 minute final extension at 72°C. Following amplification, shrimp alkaline phosphatase (SAP) (0.3 units in a 2 µl volume) (Amersham Pharmacia) was added to each reaction (total reaction volume was 7 µl) to remove any residual dNTPs that were not consumed in the PCR step. Samples were incubated for 20 minutes at 37°C, followed by 5 minutes at 85°C to denature the SAP.

[0210] Once the SAP reaction was complete, a primer extension reaction was initiated by adding a polymorphism-specific MassEXTEND™ primer cocktail to each sample. Each MassEXTEND™ cocktail included a specific combination of dideoxynucleotides (ddNTPs) and deoxynucleotides (dNTPs) used to distinguish polymorphic alleles from one another. Methods for verifying, allelotyping and genotyping SNPs are disclosed, for example, in U.S. Pat. No. 6,258,538, the content of which is hereby incorporated by reference. In Table 4, ddNTPs are shown and the fourth nucleotide not shown is the dNTP.

TABLE 4: Extension Primers

SNP Reference	Extend Probe	Termination Mix
rs756519	CAGAGCCCTGTTCTTTGATTT	ACG
rs1042327	CATCACAGCTCCCCACCAT	ACT
rs8770	TAGACACTGTGTAAGCAATC	ACG
rs1563055	TTCTCCTCACATTGTTTCTACT	ACG
rs912428	CCATTCCAGGGAGACTCCCA	ACT
rs1888475	GACATCAAATGATTCCCCTGT	ACT

[0211] The MassEXTEND™ reaction was performed in a total volume of 9 µl, with the addition of 1X ThermoSequenase buffer, 0.576 units of ThermoSequenase (Amersham Pharmacia), 600 nM MassEXTEND™ primer, 2 mM of ddATP and/or ddCTP and/or ddGTP and/or ddTTP, and 2 mM of dATP or dCTP or dGTP or dTTP. The deoxy nucleotide (dNTP) used in the assay normally was

complementary to the nucleotide at the polymorphic site in the amplicon. Samples were incubated at 94°C for 2 minutes, followed by 55 cycles of 5 seconds at 94°C, 5 seconds at 52°C, and 5 seconds at 72°C.

[0212] Following incubation, samples were desalted by adding 16 μl of water (total reaction volume was 25 μl), 3 mg of SpectroCLEAN™ sample cleaning beads (Sequenom, Inc.) and allowed to incubate for 3 minutes with rotation. Samples were then robotically dispensed using a piezoelectric dispensing device (SpectroJET™ (Sequenom, Inc.)) onto either 96-spot or 384-spot silicon chips containing a matrix that crystallized each sample (SpectroCHIP™ (Sequenom, Inc.)). Subsequently, MALDI-TOF mass spectrometry (Biflex and Autoflex MALDI-TOF mass spectrometers (Bruker Daltonics) can be used) and SpectroTYPER RT™ software (Sequenom, Inc.) were used to analyze and interpret the SNP genotype for each sample.

Genetic Analysis

[0213] Minor allelic frequencies for the polymorphisms set forth in Table A were verified as being 10% or greater using the extension assay described above in a group of samples isolated from 92 individuals originating from the state of Utah in the United States, Venezuela and France (Coriell cell repositories).

[0214] Genotyping results are shown for female pools in Table 5. In Table 5, "AF" refers to allelic frequency; and "F case" and "F control" refer to female case and female control groups, respectively.

TABLE 5: Genotyping Results

SNP Reference	AF F case	AF F control	p-value
rs756519	C = 0.581 T = 0.419	C = 0.656 T = 0.344	0.0055
rs1042327	T = 0.472 C = 0.528	T = 0.563 C = 0.437	0.0012
rs8770	C = 0.529 T = 0.471	C = 0.432 T = 0.568	0.0001
rs1563055	C = 0.653 T = 0.347	C = 0.736 T = 0.264	0.0013
rs912428	T = 0.228 C = 0.772	T = 0.170 C = 0.830	0.0076
rs1888475	A = 0.188 G = 0.812	A = 0.135 G = 0.865	0.0087

[0215] All of the single marker alleles set forth in Table A were considered validated, since the genotyping data agreed with the allelotyping data and each SNP significantly associated with osteoarthritis. Particularly significant associations with osteoarthritis are indicated by a calculated p-value of less than 0.05 for genotype results.

Example 3

Association of Polymorphic Variants with Osteoarthritis in Replication Cohorts

[0216] The single marker polymorphisms set forth in Table A were genotyped again in two replication cohorts consisting of individuals selected for OA.

Sample Selection and Pooling Strategies – Replication Sample 1

[0217] A second case control sample (replication sample #1) was created by using 100 Caucasian female cases from Chingford, UK, and 148 unrelated female cases from the St. Thomas twin study. Cases were defined as having Kellgren-Lawrence (KL) scores of at least 2 in at least one knee x-ray. In addition, 199 male knee replacement cases from Nottingham were included. (For a cohort description, see the Nottingham description provided in Example 1). The control pool was made up of unrelated female individuals from the St. Thomas twin study (England) with normal knee x-rays and without other indications of OA, regardless of anatomical location, as well as lacking family history of OA. The St. Thomas twin study consists of Caucasian, female participants from the St. Thomas' Hospital, London, adult-twin registry, which is a voluntary registry of >4,000 twin pairs ranging from 18 to 76 years of age. The replication sample 1 cohort was used to replicate the initial results. Table 6 below summarizes the selected phenotype data collected from the case and control individuals.

TABLE 6

Phenotype	**Female cases (n=248):** median (range)/ (n,%)	**Male cases (n=199):** median (range)/ (n,%)	**Female controls (n=313):** mean (range)/ (n,%)
Age	59 (39- 73)	66 (45- 73)	55 (50- 72)
Height (cm)	162 (141- 178)	175 (152- 198)	162 (141- 176)
Weight (kg)	68 (51- 123)	86 (62- 127)	64 (40- 111)
Body mass index (kg/m^2)	26 (18- 44)	29 (21- 41)	24 (18- 46)
Kellgren-Lawrence* left knee	0 (63, 26%), 1 (20, 8%), 2 (105, 43%), 3 (58, 23%), 4 (1, 0%)	NA	NA
Kellgren-Lawrence* right knee	0 (43, 7%), 1 (18, 7%), 2 (127, 52%), 3 (57, 23%), 4 (1, 0%)	NA	NA
KL* >2 both knees	No (145, 59%), Yes (101, 41%)	NA	NA
KL* >2 either knee	No (0, 0%), Yes (248, 100%)	NA	NA

* 0: normal, 1: doubtful, 2: definite osteophyte (bony protuberance), 3: joint space narrowing (with or without osteophyte), 4: joint deformity

Sample Selection and Pooling Strategies – Replication Sample 2

[0218] A third case control sample (replication sample #2) was created by using individuals with symptoms of OA from Newfoundland, Canada. These individuals were recruited and examined by rheumatologists. Affected joints were x-rayed and a final diagnosis of definite or probable OA was made according to American College of Rheumatology criteria by a single rheumatologist to avoid any inter-examiner diagnosis variability. Controls were recruited from volunteers without any symptoms from the musculoskeletal system based on a normal joint exam performed by a rheumatologist. Only cases with a diagnosis of definite OA were included in the study. Only individuals of Caucasian origin were included. The cases consisted of 228 individuals with definite knee OA, 106 individuals with definite hip OA, and 74 individuals with hip OA.

TABLE 7

Phenotype	Case	Control
Age at Visit	62.7	52.5
Sex (Female/Male)	227/119	174/101
Knee OA Xray: No	35% (120)	80% (16)
Unknown	1% (4)	0% (0)
Yes	64% (221)	20% (4)
Hip OA Xray: No	63% (215)	80% (16)
Unknown	2% (7)	0% (0)
Yes	35% (121)	20% (4)

Assay for Verifying, Allelotyping, and Genotyping SNPs

[0219] Genotyping of the replication cohorts described in Tables 6 and 7 was performed using the same methods used for the original genotyping, as described herein. A MassARRAY™ system (Sequenom, Inc.) was utilized to perform SNP genotyping in a high-throughput fashion. This genotyping platform was complemented by a homogeneous, single-tube assay method (hME™ or homogeneous MassEXTEND™ (Sequenom, Inc.)) in which two genotyping primers anneal to and amplify a genomic target surrounding a polymorphic site of interest. A third primer (the MassEXTEND™ primer), which is complementary to the amplified target up to but not including the polymorphism, was then enzymatically extended one or a few bases through the polymorphic site and then terminated.

[0220] For each polymorphism, SpectroDESIGNER™ software (Sequenom, Inc.) was used to generate a set of PCR primers and a MassEXTEND™ primer which where used to genotype the polymorphism. Other primer design software could be used or one of ordinary skill in the art could manually design primers based on his or her knowledge of the relevant factors and considerations in

designing such primers. Table 3 shows PCR primers and Table 4 shows extension probes used for analyzing (*e.g.*, genotyping) polymorphisms in the replication cohorts. The initial PCR amplification reaction was performed in a 5 μl total volume containing 1X PCR buffer with 1.5 mM $MgCl_2$ (Qiagen), 200 μM each of dATP, dGTP, dCTP, dTTP (Gibco-BRL), 2.5 ng of genomic DNA, 0.1 units of HotStar DNA polymerase (Qiagen), and 200 nM each of forward and reverse PCR primers specific for the polymorphic region of interest.

[0221] Samples were incubated at 95°C for 15 minutes, followed by 45 cycles of 95°C for 20 seconds, 56°C for 30 seconds, and 72°C for 1 minute, finishing with a 3 minute final extension at 72°C. Following amplification, shrimp alkaline phosphatase (SAP) (0.3 units in a 2 μl volume) (Amersham Pharmacia) was added to each reaction (total reaction volume was 7 μl) to remove any residual dNTPs that were not consumed in the PCR step. Samples were incubated for 20 minutes at 37°C, followed by 5 minutes at 85°C to denature the SAP.

[0222] Once the SAP reaction was complete, a primer extension reaction was initiated by adding a polymorphism-specific MassEXTEND™ primer cocktail to each sample. Each MassEXTEND™ cocktail included a specific combination of dideoxynucleotides (ddNTPs) and deoxynucleotides (dNTPs) used to distinguish polymorphic alleles from one another. Methods for verifying, allelotyping and genotyping SNPs are disclosed, for example, in U.S. Pat. No. 6,258,538, the content of which is hereby incorporated by reference. In Table 7, ddNTPs are shown and the fourth nucleotide not shown is the dNTP.

[0223] The MassEXTEND™ reaction was performed in a total volume of 9 μl, with the addition of 1X ThermoSequenase buffer, 0.576 units of ThermoSequenase (Amersham Pharmacia), 600 nM MassEXTEND™ primer, 2 mM of ddATP and/or ddCTP and/or ddGTP and/or ddTTP, and 2 mM of dATP or dCTP or dGTP or dTTP. The deoxy nucleotide (dNTP) used in the assay normally was complementary to the nucleotide at the polymorphic site in the amplicon. Samples were incubated at 94°C for 2 minutes, followed by 55 cycles of 5 seconds at 94°C, 5 seconds at 52°C, and 5 seconds at 72°C.

[0224] Following incubation, samples were desalted by adding 16 μl of water (total reaction volume was 25 μl), 3 mg of SpectroCLEAN™ sample cleaning beads (Sequenom, Inc.) and allowed to incubate for 3 minutes with rotation. Samples were then robotically dispensed using a piezoelectric dispensing device (SpectroJET™ (Sequenom, Inc.)) onto either 96-spot or 384-spot silicon chips containing a matrix that crystallized each sample (SpectroCHIP™ (Sequenom, Inc.)). Subsequently, MALDI-TOF mass spectrometry (Biflex and Autoflex MALDI-TOF mass spectrometers (Bruker Daltonics) can be used) and

SpectroTYPER RT™ software (Sequenom, Inc.) were used to analyze and interpret the SNP genotype for each sample.

Genetic Analysis

[0225] Genotyping results for replication cohorts #1 and #2 are provided in Tables 8 and 9, respectively.

TABLE 8

rsID	Replication #1 (Mixed Male/Female cases and Female controls)				Meta-analysis Disc. + Rep #1
	AF OA Con	AF OA Cas	Delta	P-value	P-value
rs756519	0.4	0.43	-0.04	0.140	0.0098
rs1042327	0.49	0.52	-0.03	0.234	0.0430
rs8770	0.51	0.48	0.03	0.303	0.0480
rs1563055	0.31	0.35	-0.04	0.083	0.0002
rs912428	0.86	0.8	0.06	**0.004**	~0.00001
rs1888475	0.86	0.81	0.04	0.032	0.0002

TABLE 9

rsID	Replication #2 (Newfoundland) (Male/Female cases and controls)				Meta-analysis Disc. + Rep #2
	AF OA Con	AF OA Cas	Delta	P-value	Not Done
rs756519	0.39	0.40	-0.007	0.816	
rs1042327	0.49	0.51	-0.024	0.405	
rs8770	0.53	0.49	0.039	0.195	
rs1563055	0.34	0.34	-0.005	0.864	
rs912428	0.82	0.76	0.058	**0.016**	
rs1888475	0.80	0.82	-0.025	0.280	

[0226] To combine the evidence for association from multiple sample collections, a meta-analysis procedure was employed. The allele frequencies were compared between cases and controls within the discovery sample, as well as within the replication cohort #1 using the DerSimian-Laird approach (DerSimonian, R. and N. Laird. 1986. Meta-analysis in clinical trials. Control Clin Trials 7: 177-188.)

[0227] The absence of a statistically significant association in one or more of the replication cohorts should not be interpreted as minimizing the value of the original finding. There are many reasons why a biologically derived association identified in a sample from one population would not replicate in a sample from another population. The most important reason is differences in population history. Due to bottlenecks and founder effects, there may be common disease predisposing alleles present in one population that are relatively rare in another, leading to a lack of association in the candidate region. Also, because common diseases such as arthritis-related disorders are the result of susceptibilities in

many genes and many environmental risk factors, differences in population-specific genetic and environmental backgrounds could mask the effects of a biologically relevant allele. For these and other reasons, statistically strong results in the original, discovery sample that did not replicate in one or more of the replication samples may be further evaluated in additional replication cohorts and experimental systems.

Example 4

Chromosome 6 Region Proximal SNPs

[0228] It has been discovered that SNPs rs756519, rs1042327 and rs8770 on chromosome 6 (6q27) are associated with occurrence of osteoarthritis in subjects. This region contains genes that encode proteasome (prosome, macropain) subunit, beta type, 1 (*PSMB1*), TATA box binding protein (*TBP*), and programmed cell death 2 (*PDCD2*).

[0229] One hundred-nine additional allelic variants proximal to rs756519, rs1042327 and rs8770 were identified and subsequently allelot0yped in osteoarthritis case and control sample sets as described in Examples 1 and 2. The polymorphic variants are set forth in Table 10. The chromosome positions provided in column four of Table 10 are based on Genome "Build 34" of NCBI's GenBank.

TABLE 10

dbSNP rs#	Chromosome	Position in SEQ ID NO: 1	Chromosome Position	Allele Variants
rs1474555	6	229	170689279	c/t
rs1474554	6	6310	170695360	a/g
rs10334	6	11840	170700890	g/t
rs10541	6	11870	170700920	a/t
rs3823299	6	12064	170701114	a/g
Rs742348	6	13392	170702442	c/g
rs1474644	6	16354	170705404	a/g
rs1474643	6	16559	170705609	c/t
rs2056970	6	16935	170705985	a/g
rs2223474	6	17616	170706666	c/t
rs2206284	6	17737	170706787	c/t
Rs756519	6	18321	170707371	c/t
Rs756518	6	18453	170707503	a/g
Rs756517	6	18811	170707861	c/t
rs1474642	6	20020	170709070	c/t
rs2038093	6	21662	170710712	c/g
rs2038092	6	23197	170712247	c/g
rs2223473	6	23446	170712496	g/t
Rs760909	6	24339	170713389	g/t
rs2076319	6	25504	170714554	a/g
rs3778589	6	27174	170716224	a/g
rs3800236	6	28008	170717058	a/t

dbSNP rs#	Chromosome	Position in SEQ ID NO: 1	Chromosome Position	Allele Variants
rs2206286	6	29294	170718344	c/t
rs12717	6	29759	170718809	c/g
rs2179373	6	30832	170719882	a/g
rs3800235	6	44512	170733562	a/c
rs3823298	6	44850	170733900	c/g
rs2076318	6	45884	170734934	a/g
rs2235506	6	46345	170735395	c/t
rs2072916	6	48589	170737639	a/g
rs3734763	6	53371	170742421	a/g
rs3177571	6	53911	170742961	g/t
rs8770	6	53990	170743040	a/g
rs3173219	6	55152	170744202	c/g
Rs960744	6	55667	170744717	c/t
rs2066954	6	58952	170748002	a/c
rs2072917	6	59315	170748365	g/t
rs3173220	6	60029	170749079	a/g
Rs734249	6	61477	170750527	a/c
rs2092310	6	62988	170752038	c/t
rs2092309	6	63090	170752140	c/g
rs1016536	6	64021	170753071	a/c
rs2235506	6	65685	170754735	c/t
rs2076998	6	70220	170759270	a/g
rs2076997	6	70323	170759373	a/c
rs2345478	6	70959	170760009	a/c
rs2021899	6	73436	170762486	c/g
rs2021898	6	82945	170771995	a/g
rs2345682	6	82958	170772008	g/t
rs2345683	6	82961	170772011	c/g
rs2881195	6	82964	170772014	c/t
rs2345684	6	82965	170772015	g/t
rs3046261	6	83006	170772056	-/cttt
rs4083413	6	83025	170772075	c/t
rs4083412	6	83034	170772084	a/g
rs2345685	6	83074	170772124	g/t
rs2021897	6	83132	170772182	g/t
rs4036211	6	83155	170772205	c/t
rs4036212	6	83172	170772222	a/t
rs4036213	6	83174	170772224	g/t
rs2345686	6	83206	170772256	c/t
rs4036214	6	83216	170772266	g/t
rs4036215	6	83234	170772284	g/t
rs2345687	6	83252	170772302	a/g
rs2345688	6	83260	170772310	a/c
rs2881196	6	83263	170772313	a/c
rs3046288	6	83296	170772346	-/at
rs4036216	6	83319	170772369	a/g
rs4036205	6	83322	170772372	c/g

dbSNP rs#	Chromosome	Position in SEQ ID NO: 1	Chromosome Position	Allele Variants
rs2092307	6	83324	170772374	a/c
rs4036206	6	83357	170772407	c/g
rs2345689	6	83375	170772425	c/t
rs2345690	6	83381	170772431	c/t
rs2345691	6	83389	170772439	a/t
rs2345692	6	83443	170772493	a/g
rs3046306	6	83499	170772549	-/ggtg
rs4036207	6	83545	170772595	c/t
rs2345693	6	83566	170772616	c/t
rs2345694	6	83591	170772641	c/t
rs2345695	6	83619	170772669	g/t
rs2345696	6	83698	170772748	a/g
rs4036209	6	83780	170772830	g/t
rs2345697	6	83784	170772834	g/t
rs2881197	6	83826	170772876	g/t
rs2345698	6	83832	170772882	c/t
rs2345699	6	83852	170772902	c/t
rs2744640	6	86297	170775347	c/t
rs2744639	6	86315	170775365	g/t
rs2744638	6	86420	170775470	c/g
rs2744637	6	86460	170775510	c/g
rs2744636	6	86714	170775764	c/t
rs2744635	6	86718	170775768	c/t
rs2744634	6	86736	170775786	c/g
rs2744633	6	86753	170775803	c/t
rs2744632	6	86766	170775816	g/t
rs2744630	6	88162	170777212	c/g
rs2744629	6	88218	170777268	a/g
rs2744628	6	88246	170777296	a/g
rs2744627	6	88255	170777305	c/t
rs2977616	6	88309	170777359	g/t
rs2977617	6	88310	170777360	a/t
rs2744626	6	88471	170777521	a/g
rs2744625	6	88619	170777669	c/t
rs3115847	6	88904	170777954	c/t
rs2744623	6	89044	170778094	c/g
rs4036193	6	90531	170779581	-/aaaaa
rs4036194	6	90534	170779584	a/g
rs4036196	6	90613	170779663	c/g
Rs1042327	6	46252	170735302	c/t

Assay for Verifying and Allelotyping SNPs

[0230] The methods used to verify and allelotype the 109 proximal SNPs of Table 10 are the same methods described in Examples 1 and 2 herein. The primers and probes used in these assays are provided in Table 11 and Table 12, respectively.

TABLE 11

dbSNP rs#	Forward PCR primer	Reverse PCR primer
Rs1474555	ACGTTGGATGACATCAACTGAAGCCGACAG	ACGTTGGATGAATGGTGGAATGTGATGAGA
Rs1474554	ACGTTGGATGATACACCTAGGACACCTCCA	ACGTTGGATGCAGAAGGAGATAAACCCAGC
rs10334	ACGTTGGATGAACAGTTTCCTCCCTGATGC	ACGTTGGATGCGGCTGGTGAAAGATGTCTT
rs10541	ACGTTGGATGACTATGCAGATCCGGAGTGC	ACGTTGGATGGTCCTTGGACAGAGCCATG
Rs3823299	ACGTTGGATGCTCATGTGTACGAGGATTTG	ACGTTGGATGGTCTGGAAGGGTCTTTATTC
rs742348	ACGTTGGATGTGTGGATTTTCCAGTGCTCG	ACGTTGGATGCTGTACTTGAACTCCCAAGC
Rs1474644	ACGTTGGATGGCAAGACAAGCATAATTGGG	ACGTTGGATGTAAAGGGCATTTTGGCTTCC
Rs1474643	ACGTTGGATGTCTCCCAAATTAAAAGTGGC	ACGTTGGATGGATACCAAAGTCCTACTTAC
Rs2056970	ACGTTGGATGTGGGACTACAGGAAGAGAAG	ACGTTGGATGCAAAACACAGACCTTCAGCC
Rs2223474	ACGTTGGATGCCAGGGTAAAGAAAAGATCC	ACGTTGGATGAGAGGCTTACCTCCTAAAAG
Rs2206284	ACGTTGGATGTCACATACTAGGTGGATCCC	ACGTTGGATGAAAGAGGAGAACACAGGATG
rs756519	ACGTTGGATGTCTAGAGACACCTGAGGTTG	ACGTTGGATGTGTTTCACTTCAGAGCCCTG
rs756518	ACGTTGGATGCCCAGATTAGACTCTCTAAC	ACGTTGGATGAAATAGCTGAGCTGCCATTG
rs756517	ACGTTGGATGCTCGGTTGTTGACTCCTATC	ACGTTGGATGGCGGATGTTAAGAGTCAGAG
Rs1474642	ACGTTGGATGGGAGGTCATACATTAGCTTC	ACGTTGGATGTACCATCTGACACAATTCTC
Rs2038093	ACGTTGGATGGAGACAGAGTTTCACTCTTG	ACGTTGGATGTAATCACTTGAACCCAGGAG
Rs2038092	ACGTTGGATGTTACCTGAGGTCAGGAGTTT	ACGTTGGATGCCACACCCAGCTGATTTTTG
Rs2223473	ACGTTGGATGCCTTTATGTTATTGCTTTCC	ACGTTGGATGCAGGGAAATTTAAGAATAGC
rs760909	ACGTTGGATGGGAAGAGGCAAGCTTAGTTC	ACGTTGGATGGCAGCATTAACGAATGCCTG
Rs2076319	ACGTTGGATGGACATTTCACAATGCCTTTG	ACGTTGGATGCCAACAGCAACTTAAAAACTC
Rs3778589	ACGTTGGATGGCAAGAGAGAGAAAAGTTCC	ACGTTGGATGGTGTTTCTGTCCCATTTCAC
Rs3800236	ACGTTGGATGAGAGAATGAGGCCTCATTTT	ACGTTGGATGCTCAGTCATTGTTCTTTTTC
Rs2206286	ACGTTGGATGTTCAGACGCTAACCCTCTAC	ACGTTGGATGAACATAGCCTCTGCTCTGTG
rs12717	ACGTTGGATGAAAATCGCAGCTGCAAAGGG	ACGTTGGATGAGACAGCAAGTGTCGGATCC
Rs2179373	ACGTTGGATGGAAGTGACCTATGCTCACAC	ACGTTGGATGAATGTCACTTCCGCCAGTTC
Rs3800235	ACGTTGGATGCTATGTGTTGATACCTCCAAG	ACGTTGGATGGCTTCATAAATGAACTGAAC
Rs3823298	ACGTTGGATGGGTGGTTTCTTGTCTTGATG	ACGTTGGATGTTTTTGTCCCAGAGCATCTG
Rs2076318	ACGTTGGATGTCCGCCAAATTATTGTAGCC	ACGTTGGATGCTCAGTAGAAATGCATGGGC
Rs2235506	ACGTTGGATGTAACCATGTCAACTGTTCTC	ACGTTGGATGCCCACCAACAATTTAGTAGG
Rs2072916	ACGTTGGATGACGCTGGAGTCACTAAGATG	ACGTTGGATGCAGATTAAGGCACAGGCATG
Rs3734763	ACGTTGGATGGCCTTTTGCCTTTCAGTGTC	ACGTTGGATGTAAAGAGGCTGGACCTTCAG
Rs3177571	ACGTTGGATGGTCTGTTGTCAATATAGGTG	ACGTTGGATGACAAAAGTGTCCAGTGACAG
rs8770	ACGTTGGATGAATTCCCTGTCACTGGACAC	ACGTTGGATGCCAAAAATAGAGGTGCAGAG
Rs3173219	ACGTTGGATGACATAACCACACTGGAGGTG	ACGTTGGATGCCTAGTTTTCAGACACGGTC
rs960744	ACGTTGGATGAAAGGCATGTCACAGTTCCC	ACGTTGGATGGCCCTCTGAGTCAGATAAAC
Rs2066954	ACGTTGGATGGAGGTTCTGGGTATAACTTTC	ACGTTGGATGCTACAAACCAGTAAGCTGATG
Rs2072917	ACGTTGGATGTGCTAGGCACTCACACTATC	ACGTTGGATGAGGCTTGGTAAGTTCCTCTG
Rs3173220	ACGTTGGATGTATCTGGGTTGACAAAGGCG	ACGTTGGATGACATAAGCAGGCTTGTGCAC
rs734249	ACGTTGGATGAGGTGGACACCAGCAGGGAA	ACGTTGGATGTCACCTCTGCACATGTCTTG

dbSNP rs#	Forward PCR primer	Reverse PCR primer
Rs2092310	ACGTTGGATGTTAGTCAGGTAAAGCGGGAC	ACGTTGGATGTCAGTGGAAGGCTGATCAAG
Rs2092309	ACGTTGGATGATCTAATTGCTTCCCCTCCC	ACGTTGGATGCAGCCTTCCACTGAATACAC
Rs1016536	ACGTTGGATGCCCCAAAAATTGGAGACAGG	ACGTTGGATGGGCTGTCATAATCGTGTGTC
Rs2235506	ACGTTGGATGAAGTGATTCTCCTGCCTCAG	ACGTTGGATGTGGTGAAACCCTGTCTCTAC
Rs2076998	ACGTTGGATGGCTCTGTGATTTCGATGATG	ACGTTGGATGAGCTACTTCTTGCAGGAGTC
Rs2076997	ACGTTGGATGCAGAGCTTCCAAGTGTTTTC	ACGTTGGATGAAAGGAGTGCTTAAAGGAGC
Rs2345478	ACGTTGGATGCCTTCAACAAGTGCTGACAC	ACGTTGGATGATCCAGGCATTATTGCCAGC
Rs2021899	ACGTTGGATGGTTTTGTGGTGGATGATGGG	ACGTTGGATGAGAGTGCCCATAATGGACAG
Rs2021898	ACGTTGGATGCGCAAGAAACTCCTTGGATG	ACGTTGGATGCCAATTAAAGCCAAGGTCAC
Rs2345682	ACGTTGGATGATTCGCAAGAAACTCCTTGG	ACGTTGGATGGGAAGAAATCTTACCAGAAC
Rs2345683	ACGTTGGATGATTCGCAAGAAACTCCTTGG	ACGTTGGATGGGAAGAAATCTTACCAGAAC
Rs2881195	ACGTTGGATGATTCGCAAGAAACTCCTTGG	ACGTTGGATGGGAAGAAATCTTACCAGAAC
Rs2345684	ACGTTGGATGATTCGCAAGAAACTCCTTGG	ACGTTGGATGGGAAGAAATCTTACCAGAAC
Rs3046261	ACGTTGGATGCTCCACTCAGACATCAAAAG	ACGTTGGATGGTGACCTTGGCTTTAATTGG
Rs4083413	ACGTTGGATGGTGACCTTGGCTTTAATTGG	ACGTTGGATGCTCCACTCAGACATCAAAAG
Rs4083412	ACGTTGGATGGTGACCTTGGCTTTAATTGG	ACGTTGGATGCTCCACTCAGACATCAAAAG
Rs2345685	ACGTTGGATGGTTCTGGTAAGATTTCTTCC	ACGTTGGATGAGTCTTACAATAGATGACTG
Rs2021897	ACGTTGGATGGCAATTATTTACAGAAGCCC	ACGTTGGATGTCCCACACAGTCATCTATTG
Rs4036211	ACGTTGGATGCCCATTACAAGTTGGGCAGTT	ACGTTGGATGCTTTCTGATTCCTTTTTTTTCC
Rs4036212	ACGTTGGATGCTTTCTGATTCCTTTTTTTCC	ACGTTGGATGCCCATTACAAGTTGGGCAGTT
Rs4036213	ACGTTGGATGCCCATTACAAGTTGGGCAGTT	ACGTTGGATGCTTTCTGATTCCTTTTTTTCC
Rs2345686	ACGTTGGATGCCCATTACAAGTTGGGCAGTT	ACGTTGGATGCTTTCTGATTCCTTTTTTTCC
Rs4036214	ACGTTGGATGCCCATTACAAGTTGGGCAGTT	ACGTTGGATGCTTTCTGATTCCTTTTTTTCC
Rs4036215	ACGTTGGATGCTTTCTGATTCCTTTTTTTCC	ACGTTGGATGCCCATTACAAGTTGGGCAGTT
Rs2345687	ACGTTGGATGGGATTGTAAGGTGAGACTTG	ACGTTGGATGTTCCTCCCCATTACAAGTTG
Rs2345688	ACGTTGGATGAGGGTCCCATCTAAGAATTC	ACGTTGGATGGGATTGTAAGGTGAGACTTG
Rs2881196	ACGTTGGATGAGGGTCCCATCTAAGAATTC	ACGTTGGATGGGATTGTAAGGTGAGACTTG
Rs3046288	ACGTTGGATGCCAACTTGTAATGGGGAGGA	ACGTTGGATGCAGTTTTTACAGAGGGTCCC
Rs4036216	ACGTTGGATGCTTGTAATGGGGAGGAAAAAA	ACGTTGGATGTTCTCATTTTAATCTGTCAG
Rs4036205	ACGTTGGATGCTTGTAATGGGGAGGAAAAAA	ACGTTGGATGTTCTCATTTTAATCTGTCAG
Rs2092307	ACGTTGGATGCTTGTAATGGGGAGGAAAAAA	ACGTTGGATGTTCTCATTTTAATCTGTCAG
Rs4036206	ACGTTGGATGGACCCTCTGTAAAAACTGAC	ACGTTGGATGCCACTGCACCTCAAATCTTC
Rs2345689	ACGTTGGATGTTCCCTGAGTATCTCCCATG	ACGTTGGATGGGGACCCTCTGTAAAAACTG
Rs2345690	ACGTTGGATGTTCCCTGAGTATCTCCCATG	ACGTTGGATGGGGACCCTCTGTAAAAACTG
Rs2345691	ACGTTGGATGGCCACCTGTTGGAGATTTAC	ACGTTGGATGGGGACCCTCTGTAAAAACTG
Rs2345692	ACGTTGGATGTACATGGGAGATACTCAGGG	ACGTTGGATGCCACTGCACCTCAAATCTTC
Rs3046306	ACGTTGGATGGTATAACAAACCTTACCCTTG	ACGTTGGATGTAAAGAAAGAAGATTTGAGG
Rs4036207	ACGTTGGATGTATCAATGGAGAATGCGTGG	ACGTTGGATGGGGAGTTAACCAGCAAAAGC
Rs2345693	ACGTTGGATGTCGACAACAAGAAGAGAAGG	ACGTTGGATGCACATTAGACAAGGGTAAGG
Rs2345694	ACGTTGGATGCTACCTCTCTCGACAACAAG	ACGTTGGATGCTTAAGTCCACGCATTCTCC
Rs2345695	ACGTTGGATGCGCATTCTCCATTGATAAGAC	ACGTTGGATGCCATTTAAAAGCTACCTCTC
Rs2345696	ACGTTGGATGCCTTACACAAGTGTAACTTC	ACGTTGGATGCCCCAAAATATAATGGTAGG
Rs4036209	ACGTTGGATGGGAACACAGTGTATAAGACC	ACGTTGGATGGTTTTCACAACTTCGTTAGC
Rs2345697	ACGTTGGATGGTTTTCACAACTTCGTTAGC	ACGTTGGATGGCCACCCCAAAATATAATGG
Rs2881197	ACGTTGGATGGCTGGAGGAAAAACAAGAAC	ACGTTGGATGCCTACCATTATATTTTGGGG
Rs2345698	ACGTTGGATGCTGGAGGAAAAACAAGAACTC	ACGTTGGATGCATTATATTTTGGGGTGGCAT
Rs2345699	ACGTTGGATGGCTGGAGGAAAAACAAGAAC	ACGTTGGATGGGGTGGCATATTTTGGTCTT

dbSNP rs#	Forward PCR primer	Reverse PCR primer
Rs2744640	ACGTTGGATGGCAACAGCACTTAGTATGCC	ACGTTGGATGTGTGAAGCTGCAAATCTGGC
Rs2744639	ACGTTGGATGGCAACAGCACTTAGTATGCC	ACGTTGGATGTGTGAAGCTGCAAATCTGGC
Rs2744638	ACGTTGGATGAACCGTGGCAATACCACGTC	ACGTTGGATGTGGGTTTGGGCTGGATTTGG
Rs2744637	ACGTTGGATGTGAGTTGACAGCCTCTGCTGG	ACGTTGGATGCACGTCAGTAAGGCAGAGAC
Rs2744636	ACGTTGGATGTCGGAGATGACATTGTCACC	ACGTTGGATGTTCCAGGGGTTACGTGTGTG
Rs2744635	ACGTTGGATGTGAGTCTGACTGTGTCACGG	ACGTTGGATGTCGGAGATGACATTGTCACC
Rs2744634	ACGTTGGATGCGTGTTCCAGGGATTATATG	ACGTTGGATGGCACATAACGCTTGGAACTC
Rs2744633	ACGTTGGATGTATGAGTGTGACGGGTGTAG	ACGTTGGATGGCACATAACGCTTGGAACTC
Rs2744632	ACGTTGGATGTAGCTGCCTTCCACATCCAA	ACGTTGGATGTGTGACGGGTGTAGCGTTAG
Rs2744630	ACGTTGGATGGGGTTCAAATGCCTCTGATAG	ACGTTGGATGGGTCTAGGACAAGACCCATT
Rs2744629	ACGTTGGATGAACTTTCCCTTAGCCAGTGG	ACGTTGGATGATCAGAGGCATTTGAACCCC
Rs2744628	ACGTTGGATGTTGACCTCAAATCATGTCAC	ACGTTGGATGTATCAGAGGCATTTGAACCC
Rs2744627	ACGTTGGATGGGGTGGTTTATGTTCCACTG	ACGTTGGATGCCAGAACTAATGCTAGCTTC
Rs2977616	ACGTTGGATGTTCCACTGGCTAAGAGAAAG	ACGTTGGATGCCAGAACTAATGCTAGCTTC
Rs2977617	ACGTTGGATGCCAGAACTAATGCTAGCTTC	ACGTTGGATGTTCCACTGGCTAAGAGAAAG
Rs2744626	ACGTTGGATGACAGTGAAATTGTATTTCCG	ACGTTGGATGGCACAAACTTAAGAATCTCC
Rs2744625	ACGTTGGATGAGCAAAATCCACCTATGTCC	ACGTTGGATGCTGAATTTTGTCTCCAGTAC
Rs3115847	ACGTTGGATGTCGAGGCAGAGGCGTAGTA	ACGTTGGATGATAGGAATGACATGAACCCG
Rs2744623	ACGTTGGATGACGCGAGTCCGTAGGTGCTG	ACGTTGGATGAAGAGGCTGCTACCCAGAG
Rs4036193	ACGTTGGATGAGAGCAAGACTCCGTCTCAA	ACGTTGGATGACATGTCGCTTGATGTGTGC
Rs4036194	ACGTTGGATGACATGTCGCTTGATGTGTGC	ACGTTGGATGAGAGCAAGACTCCGTCTCAA
Rs4036196	ACGTTGGATGCCCCAGCGTTCATATTTGTC	ACGTTGGATGTCTGGCCAAATGGTCATACC
rs1042327	ACGTTGGATGAACTTCACATCACAGCTCCC	ACGTTGGATGCAGAAGTTGGGTTTTCCAGC

TABLE 12

dbSNP rs#	Extend Primer	Term Mix
rs1474555	TGAAGCCGACAGTGACACC	ACT
rs1474554	CCAATTTTGCACACCTCCAGCA	ACG
rs10334	CAGATCCGGAGTGCGTCC	CGT
rs10541	TCTCTCTCAGCCGCAGAA	CGT
rs3823299	GAGGATTTGTGATGAAAATACTA	ACG
rs742348	AATCCCCGTGTTGTTCAAGG	ACT
rs1474644	AAGGATGTTCATCATAGTGTTTA	ACG
rs1474643	ACATGTTTATACATACACTCATG	ACG
rs2056970	TTGGCAGCTTTTTAGGCCTC	ACT
rs2223474	AAGTCTCAAAAAGGTCCC	ACT
rs2206284	TAGGTGGATCCCTTTTCCC	ACG
rs756519	CAGAGCCCTGTTCTTTGATTT	ACG
rs756518	CAAAGGATGCTGTCTGGCC	ACG
rs756517	GTTCCATGAGCGTTTTCTTTG	ACG
rs1474642	CTTCAGTTTCTTCATCACTTTC	ACT
rs2038093	TTTCACTCTTGTTGCCCAGG	ACT
rs2038092	CCAACATGGTGAAACCCCATCT	ACT
rs2223473	TAGAATTAAAATTAGACTTTGGGG	ACT

dbSNP rs#	Extend Primer	Term Mix
rs760909	GCAAGCTTAGTTCTAGGTCAG	CGT
rs2076319	TCACAATGCCTTTGTAATGATTT	ACT
rs3778589	GTTTTAGGAAGACTGCTCTGACAA	ACG
rs3800236	CTGAGAGCCAGCTGCAGTAA	CGT
rs2206286	CCTCGCCGGCTGGCATAA	ACT
rs12717	CCATCCCCAAGTCTCTGCCAG	ACT
rs2179373	TGACCTATGCTCACACTTCTCA	ACG
rs3800235	GTGTTGATACCTCCAAGTACATTT	CGT
rs3823298	CTTGATGAAATAGTCATCCAACTA	ACT
rs2076318	TGAATTATCACCATCATCA	ACT
rs2235506	TGTTGCCAATAACAATCA	ACG
rs2072916	TGTGACAAGGGATTCCAC	ACG
rs3734763	CATCTGTAAGCAGGGCCGC	ACG
rs3177571	AAGACTGTGTAGCCTTCCTCTG	ACT
rs8770	GTAGACACTGTGTAAGCAATC	ACG
rs3173219	CACTGGAGGTGGAGAGCA	ACT
rs960744	CCCCATCAGACCTGGCTGT	ACT
rs2066954	TTACAATTTGAGCCTTGAGC	CGT
rs2072917	CTATCCCGACCCGAGAAAC	CGT
rs3173220	GCGATGAAACTGAACTGA	ACT
rs734249	CACCAGCAGGGAAGGTTTG	CGT
rs2092310	TTGAGGTGAGGGCTTCCAG	ACT
rs2092309	TCCCCTCCCCTATTGTTTAC	ACT
rs1016536	AAATTGGAGACAGGTCTCAGT	ACT
rs2235506	CTGGGAGTACAGGTGCGC	ACT
rs2076998	GTTTTTGTATAGTCTGCAGATGC	ACT
rs2076997	ATCCATTTTAATGGGTTGCTAGCT	ACT
rs2345478	ACAACTGTACTTATTGGGCATA	ACT
rs2021899	CTTTCTTGGAAACTCTTCCCA	ACT
rs2021898	TTGGATGGGGTTAATGGCAG	ACG
rs2345682	GTTAATGGCAGCTGTATTTTTCTG	ACT
rs2345683	GGCAGCTGTATTTTTCTGTGA	ACT
rs2881195	CAGCTGTATTTTTCTGTGACCT	ACG
rs2345684	GCAGCTGTATTTTTCTGTGACCTT	ACT
rs3046261	GAAAACATTTGAGATACTGAAGAT	ACT
rs4083413	TTCCTTTATCTTCAGTATCTCAA	ACT
rs4083412	TCTTCAGTATCTCAAATGTTTTCA	ACG
rs2345685	CAACTTTTGATGTCTGAGTGGA	ACT
rs2021897	ATTATTTACAGAAGCCCTATTCA	ACT
rs4036211	TTTCCAAACAAAAGCTACCATGCA	ACT
rs4036212	AAATAATTGCATGGTAGCTTTTG	CGT
rs4036213	ACAACTACTTTGATGTTATTTCC	CGT
rs2345686	ACAATCCAAAAATCACATTCCTA	ACT
rs4036214	GTCTCACCTTACAATCCAAAAAT	CGT

dbSNP rs#	Extend Primer	Term Mix
rs4036215	AATGTGATTTTTGGATTGTAAGG	ACT
rs2345687	AAGGTGAGACTTGTTTAGCTTT	ACT
rs2345688	TCCTCCCCATTACAAGTTGGGCA	ACT
rs2881196	TTTTCCTCCCCATTACAAGTTGG	ACT
rs3046288	TAATGGGGAGGAAAAAAATTTTCT	ACT
rs4036216	ATGTTTTTGGAATTCTTAGATGG	ACT
rs4036205	GTTTTTGGAATTCTTAGATGGGAC	ACT
rs2092307	TGGAATTCTTAGATGGGACCC	ACT
rs4036206	ACTGACAGATTAAAATGAGAAAAA	ACT
rs2345689	TCCCATGTATCCATAAGGTATAC	ACT
rs2345690	GTATCTCCCATGTATCCATAAG	ACT
rs2345691	CCCTGAGTATCTCCCATGTA	CGT
rs2345692	TCTCCAACAGGTGGCTTTCA	ACT
rs3046306	TTGCTGGTTAACTCCCCACT	CGT
rs4036207	GCGTGGACTTAAGTCTGTATAAC	ACT
rs2345693	AGAGTCTTATCAATGGAGAATGC	ACT
rs2345694	GAAGAGAAGGATAACTAAATCACT	ACT
rs2345695	ATTTAGTTATCCTTCTCTTCTTG	ACT
rs2345696	ACACAAGTGTAACTTCTACTCT	ACT
rs4036209	GGAAACCAGAATATGCCACC	CGT
rs2345697	AGCCAAAGGGACATATTTTGTGGT	ACT
rs2881197	GGAACACAGTGTATAAGACCAAA	CGT
rs2345698	CGGTGGAACACAGTGTATAAG	ACT
rs2345699	AAAACAAGAACTCTTTTCATTGCC	ACT
rs2744640	TTTATCTCCAGTTCCCCAGC	ACG
rs2744639	AGCACTTAGTATGCCTTCTCCTT	ACT
rs2744638	TGGCAATACCACGTCAGTAAG	ACT
rs2744637	GCTGGGCTGGGTTTGGGCTG	ACT
rs2744636	ACCCGTCACACTCATATAATCCC	ACG
rs2744635	ACACATGCGTGTTCCAGGG	ACT
rs2744634	GGGATTATATGAGTGTGACGG	ACT
rs2744633	GGGTGTAGCGTTAGGTGAC	ACT
rs2744632	GCGCACATAACGCTTGGAAC	ACT
rs2744630	CGTGTTAAAACTCATGGCCAAAC	ACT
rs2744629	ATAAACCACCCTGGAGTTCAT	ACT
rs2744628	TTGAAGAAAACTTTCCCTTAGCCA	ACT
rs2744627	GTTTATGTTCCACTGGCTAAG	ACT
rs2977616	TTGAGGTCAAACATTAATATCAAG	ACT
rs2977617	CTAGCTTCTCAATCTTTTGAGTT	CGT
rs2744626	GTGAAATTGTATTTCCGGATTTC	ACT
rs2744625	TCCTGAACACTTATCCACTTTAC	ACT
rs3115847	CCAGGGCTGGAGGGGCC	ACT
rs2744623	GGTGCTGGCGGGAGCGAGAGT	ACT
rs4036193	GACTCCGTCTCAAAAAAAAAAAA	ACT

dbSNP rs#	Extend Primer	Term Mix
rs4036194	CTTGATGTGTGCTTCAGGGTA	ACG
rs4036196	CAGTGCAAGTAAAGAGCCTTA	ACT
rs1042327	CATCACAGCTCCCCACCAT	ACT

Genetic Analysis

[0231] Allelotyping results from the discovery cohort are shown for cases and controls in Table 13. The allele frequency for the A2 allele is noted in the fifth and sixth columns for osteoarthritis case pools and control pools, respectively, where "AF" is allele frequency. The allele frequency for the A1 allele can be easily calculated by subtracting the A2 allele frequency from 1 (A1 AF = 1-A2 AF). For example, the SNP rs1474555 has the following case and control allele frequencies: case A1 (C) = 0.64; case A2 (T) = 0.36; control A1 (C) = 0.70; and control A2 (T) = 0.30, where the nucleotide is provided in paranthesis. Some SNPs are labeled "untyped" because of failed assays.

TABLE 13

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
Rs1474555	229	170689279	C/T	0.36	0.30	**0.024**
Rs1474554	6310	170695360	A/G	0.48	0.43	0.058
rs10334	11840	170700890	G/T			
rs10541	11870	170700920	A/T			
Rs3823299	12064	170701114	A/G	0.45	0.41	0.125
Rs742348	13392	170702442	C/G	0.46	0.44	0.275
Rs1474644	16354	170705404	A/G	0.75	0.77	0.270
Rs1474643	16559	170705609	C/T	0.45	0.40	**0.042**
Rs2056970	16935	170705985	A/G	0.36	0.33	0.242
Rs2223474	17616	170706666	C/T	0.42	0.46	0.140
Rs2206284	17737	170706787	C/T	0.37	0.35	0.493
rs756519	18321	170707371	C/T			
Rs756518	18453	170707503	A/G	0.49	0.53	0.133
Rs756517	18811	170707861	C/T			
Rs1474642	20020	170709070	C/T	0.12	0.12	0.904
Rs2038093	21662	170710712	C/G			
Rs2038092	23197	170712247	C/G			
Rs2223473	23446	170712496	G/T	0.42	0.45	0.296
Rs760909	24339	170713389	G/T	0.49	0.52	0.255
Rs2076319	25504	170714554	A/G	0.43	0.46	0.219
Rs3778589	27174	170716224	A/G	0.49	0.54	0.081
Rs3800236	28008	170717058	A/T	0.47	0.50	0.319
Rs2206286	29294	170718344	C/T	0.81	0.82	0.831
rs12717	29759	170718809	C/G	0.52	0.57	0.081
rs2179373	30832	170719882	A/G	0.58	0.62	0.089
rs3800235	44512	170733562	A/C	0.60	0.64	0.077
rs3823298	44850	170733900	C/G	0.44	0.38	**0.022**
rs2076318	45884	170734934	A/G	0.41	0.45	0.109
rs2235506	46345	170735395	C/T	0.68	0.66	0.320
rs2072916	48589	170737639	A/G	0.48	0.51	0.192
rs3734763	53371	170742421	A/G	0.50	0.54	0.142

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs3177571	53911	170742961	G/T			
rs8770	53990	170743040	A/G			
rs3173219	55152	170744202	C/G	0.49	0.53	0.056
rs960744	55667	170744717	C/T	0.39	0.35	0.179
rs2066954	58952	170748002	A/C	0.37	0.32	0.057
rs2072917	59315	170748365	G/T	0.46	0.42	0.153
rs3173220	60029	170749079	A/G			
rs734249	61477	170750527	A/C	0.48	0.40	**0.022**
rs2092310	62988	170752038	C/T			
rs2092309	63090	170752140	C/G	0.43	0.47	0.165
rs1016536	64021	170753071	A/C	0.10	0.10	0.985
rs2235506	65685	170754735	C/T			
rs2076998	70220	170759270	A/G			
rs2076997	70323	170759373	A/C	0.90	0.90	0.814
rs2345478	70959	170760009	A/C	0.09	0.09	0.947
rs2021899	73436	170762486	C/G	0.46	0.43	0.218
rs2021898	82945	170771995	A/G			
rs2345682	82958	170772008	G/T			
rs2345683	82961	170772011	C/G	0.28	0.34	**0.019**
rs2881195	82964	170772014	C/T			
rs2345684	82965	170772015	G/T			
rs3046261	83006	170772056	-/CTTT			
rs4083413	83025	170772075	C/T			
rs4083412	83034	170772084	A/G			
rs2345685	83074	170772124	G/T	0.71	0.71	0.835
rs2021897	83132	170772182	G/T			
rs4036211	83155	170772205	C/T			
rs4036212	83172	170772222	A/T			
rs4036213	83174	170772224	G/T			
rs2345686	83206	170772256	C/T			
rs4036214	83216	170772266	G/T			
rs4036215	83234	170772284	G/T			
rs2345687	83252	170772302	A/G	0.55	0.50	0.085
rs2345688	83260	170772310	A/C	0.53	0.52	0.958
rs2881196	83263	170772313	A/C			
rs3046288	83296	170772346	-/AT			
rs4036216	83319	170772369	A/G			
rs4036205	83322	170772372	C/G			
rs2092307	83324	170772374	A/C			
rs4036206	83357	170772407	C/G			
rs2345689	83375	170772425	C/T			
rs2345690	83381	170772431	C/T			
rs2345691	83389	170772439	A/T			
rs2345692	83443	170772493	A/G			
rs3046306	83499	170772549	-/GGTG	0.42	0.43	0.761
rs4036207	83545	170772595	C/T			
rs2345693	83566	170772616	C/T			
rs2345694	83591	170772641	C/T			
rs2345695	83619	170772669	G/T			
rs2345696	83698	170772748	A/G			
rs4036209	83780	170772830	G/T	0.79	0.73	0.156
rs2345697	83784	170772834	G/T			
rs2881197	83826	170772876	G/T			
rs2345698	83832	170772882	C/T			
rs2345699	83852	170772902	C/T			
rs2744640	86297	170775347	C/T	0.53	0.53	0.973
rs2744639	86315	170775365	G/T	0.40	0.40	0.789

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2744638	86420	170775470	C/G	0.39	0.39	0.941
rs2744637	86460	170775510	C/G	0.40	0.42	0.497
rs2744636	86714	170775764	C/T	0.76	0.73	0.271
rs2744635	86718	170775768	C/T	0.03	0.02	0.425
rs2744634	86736	170775786	C/G	0.96	0.94	0.436
rs2744633	86753	170775803	C/T	0.14	0.16	0.409
rs2744632	86766	170775816	G/T	0.80	0.83	0.217
rs2744630	88162	170777212	C/G			
rs2744629	88218	170777268	A/G	0.80	0.80	0.978
rs2744628	88246	170777296	A/G	0.71	0.67	0.206
rs2744627	88255	170777305	C/T	0.32	0.30	0.335
rs2977616	88309	170777359	G/T			
rs2977617	88310	170777360	A/T			
rs2744626	88471	170777521	A/G			
rs2744625	88619	170777669	C/T			
rs3115847	88904	170777954	C/T			
rs2744623	89044	170778094	C/G			
rs4036193	90531	170779581	-/AAAAA			
rs4036194	90534	170779584	A/G			
rs4036196	90613	170779663	C/G			
rs1042327	46252	170735302	C/T	0.45	0.39	**0.028**

[0232] The chromosome 6 proximal SNPs were also allelotyped in the replication cohorts using the methods described herein and the primers provided in Tables 11 and 12. The replication allelotyping results for replication cohort #1 and replication cohort #2 are provided in Tables 14 and 15, respectively.

TABLE 14

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1474555	229	170689279	C/T	0.37	0.27	**0.004**
rs1474554	6310	170695360	A/G	0.50	0.42	**0.020**
rs10334	11840	170700890	G/T			
rs10541	11870	170700920	A/T			
rs3823299	12064	170701114	A/G	0.45	0.40	0.080
rs742348	13392	170702442	C/G	0.47	0.41	0.075
rs1474644	16354	170705404	A/G	0.75	0.79	0.231
rs1474643	16559	170705609	C/T	0.46	0.39	**0.028**
rs2056970	16935	170705985	A/G	0.38	0.33	0.129
rs2223474	17616	170706666	C/T	0.41	0.48	0.052
rs2206284	17737	170706787	C/T	0.37	0.34	0.342
rs756519	18321	170707371	C/T			
rs756518	18453	170707503	A/G	0.48	0.56	**0.013**
rs756517	18811	170707861	C/T			
rs1474642	20020	170709070	C/T	0.10	0.13	0.277
rs2038093	21662	170710712	C/G			
rs2038092	23197	170712247	C/G			
rs2223473	23446	170712496	G/T	0.42	0.48	0.070
rs760909	24339	170713389	G/T	0.47	0.54	0.077
rs2076319	25504	170714554	A/G	0.41	0.49	**0.017**
rs3778589	27174	170716224	A/G	0.50	0.57	**0.035**
rs3800236	28008	170717058	A/T	0.47	0.52	0.126
rs2206286	29294	170718344	C/T	0.80	0.80	0.952

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs12717	29759	170718809	C/G	0.53	0.59	0.059
rs2179373	30832	170719882	A/G	0.57	0.64	**0.025**
rs3800235	44512	170733562	A/C	0.59	0.65	0.065
rs3823298	44850	170733900	C/G	0.46	0.36	**0.003**
rs2076318	45884	170734934	A/G	0.40	0.47	**0.017**
rs2235506	46345	170735395	C/T	0.68	0.65	0.434
rs2072916	48589	170737639	A/G	0.47	0.54	**0.026**
rs3734763	53371	170742421	A/G	0.49	0.56	0.052
rs3177571	53911	170742961	G/T			
rs8770	53990	170743040	A/G			
rs3173219	55152	170744202	C/G	0.49	0.55	0.069
rs960744	55667	170744717	C/T	0.39	0.34	0.131
rs2066954	58952	170748002	A/C	0.36	0.31	0.096
rs2072917	59315	170748365	G/T	0.46	0.41	0.070
rs3173220	60029	170749079	A/G			
rs734249	61477	170750527	A/C	0.37	NA	0.484
rs2092310	62988	170752038	C/T			
rs2092309	63090	170752140	C/G	0.43	0.49	0.102
rs1016536	64021	170753071	A/C	0.08	0.11	0.277
rs2235506	65685	170754735	C/T			
rs2076998	70220	170759270	A/G			
rs2076997	70323	170759373	A/C	0.89	0.91	0.655
rs2345478	70959	170760009	A/C	0.08	0.09	0.660
rs2021899	73436	170762486	C/G	0.48	0.42	0.081
rs2021898	82945	170771995	A/G			
rs2345682	82958	170772008	G/T			
rs2345683	82961	170772011	C/G	0.32	0.39	0.046
rs2881195	82964	170772014	C/T			
rs2345684	82965	170772015	G/T			
rs3046261	83006	170772056	-/CTTT			
rs4083413	83025	170772075	C/T			
rs4083412	83034	170772084	A/G			
rs2345685	83074	170772124	G/T	0.69	0.70	0.772
rs2021897	83132	170772182	G/T			
rs4036211	83155	170772205	C/T			
rs4036212	83172	170772222	A/T			
rs4036213	83174	170772224	G/T			
rs2345686	83206	170772256	C/T			
rs4036214	83216	170772266	G/T			
rs4036215	83234	170772284	G/T			
rs2345687	83252	170772302	A/G	0.62	NA	NA
rs2345688	83260	170772310	A/C	0.46	0.49	0.383
rs2881196	83263	170772313	A/C			
rs3046288	83296	170772346	-/AT			
rs4036216	83319	170772369	A/G			
rs4036205	83322	170772372	C/G			
rs2092307	83324	170772374	A/C			
rs4036206	83357	170772407	C/G			
rs2345689	83375	170772425	C/T			
rs2345690	83381	170772431	C/T			
rs2345691	83389	170772439	A/T			
rs2345692	83443	170772493	A/G			
rs3046306	83499	170772549	-/GGTG	0.39	0.40	0.729
rs4036207	83545	170772595	C/T			
rs2345693	83566	170772616	C/T			
rs2345694	83591	170772641	C/T			
rs2345695	83619	170772669	G/T			

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2345696	83698	170772748	A/G			
rs4036209	83780	170772830	G/T	0.79	0.73	0.156
rs2345697	83784	170772834	G/T			
rs2881197	83826	170772876	G/T			
rs2345698	83832	170772882	C/T			
rs2345699	83852	170772902	C/T			
rs2744640	86297	170775347	C/T	0.49	0.51	0.583
rs2744639	86315	170775365	G/T	0.45	0.43	0.745
rs2744638	86420	170775470	C/G	0.38	0.38	0.852
rs2744637	86460	170775510	C/G	0.35	0.40	0.216
rs2744636	86714	170775764	C/T	0.71	0.73	0.482
rs2744635	86718	170775768	C/T	0.05	0.03	0.195
rs2744634	86736	170775786	C/G	0.93	0.92	0.601
rs2744633	86753	170775803	C/T	0.19	0.20	0.681
rs2744632	86766	170775816	G/T	0.85	0.90	0.070
rs2744630	88162	170777212	C/G			
rs2744629	88218	170777268	A/G	0.78	0.79	0.891
rs2744628	88246	170777296	A/G	0.68	0.67	0.766
rs2744627	88255	170777305	C/T	0.32	0.30	0.636
rs2977616	88309	170777359	G/T			
rs2977617	88310	170777360	A/T			
rs2744626	88471	170777521	A/G			
rs2744625	88619	170777669	C/T			
rs3115847	88904	170777954	C/T			
rs2744623	89044	170778094	C/G			
rs4036193	90531	170779581	-/AAAAA			
rs4036194	90534	170779584	A/G			
rs4036196	90613	170779663	C/G			
rs1042327	46252	170735302	C/T	0.46	0.37	**0.004**

TABLE 15

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1474555	229	170689279	C/T	0.35	0.36	0.770
rs1474554	6310	170695360	A/G	0.45	0.44	0.873
rs10334	11840	170700890	G/T			
rs10541	11870	170700920	A/T			
rs3823299	12064	170701114	A/G	untyped	0.43	NA
rs742348	13392	170702442	C/G	0.45	0.47	0.600
rs1474644	16354	170705404	A/G	0.74	0.75	0.775
rs1474643	16559	170705609	C/T	0.43	0.41	0.614
rs2056970	16935	170705985	A/G	0.33	0.33	0.978
rs2223474	17616	170706666	C/T	0.44	0.43	0.944
rs2206284	17737	170706787	C/T	0.36	0.37	0.901
rs756519	18321	170707371	C/T			
rs756518	18453	170707503	A/G	0.50	0.47	0.453
rs756517	18811	170707861	C/T			
rs1474642	20020	170709070	C/T	0.15	0.11	0.147
rs2038093	21662	170710712	C/G			
rs2038092	23197	170712247	C/G			
rs2223473	23446	170712496	G/T	0.43	0.40	0.408
rs760909	24339	170713389	G/T	0.51	0.48	0.506
rs2076319	25504	170714554	A/G	0.44	0.40	0.264
rs3778589	27174	170716224	A/G	0.49	0.48	0.910

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs3800236	28008	170717058	A/T	0.48	0.46	0.670
rs2206286	29294	170718344	C/T	0.83	0.84	0.685
rs12717	29759	170718809	C/G	0.51	0.53	0.726
rs2179373	30832	170719882	A/G	0.59	0.58	0.880
rs3800235	44512	170733562	A/C	0.60	0.62	0.632
rs3823298	44850	170733900	C/G	0.41	0.41	0.945
rs2076318	45884	170734934	A/G	0.43	0.42	0.636
rs2235506	46345	170735395	C/T	0.69	0.67	0.594
rs2072916	48589	170737639	A/G	0.49	0.46	0.399
rs3734763	53371	170742421	A/G	0.51	0.51	0.888
rs3177571	53911	170742961	G/T			
rs8770	53990	170743040	A/G			
rs3173219	55152	170744202	C/G	0.48	0.51	0.493
rs960744	55667	170744717	C/T	0.38	0.37	0.738
rs2066954	58952	170748002	A/C	0.37	0.34	0.378
rs2072917	59315	170748365	G/T	0.45	0.45	0.982
rs3173220	60029	170749079	A/G			
rs734249	61477	170750527	A/C	0.46	0.02	
rs2092310	62988	170752038	C/T			
rs2092309	63090	170752140	C/G	0.43	0.44	0.891
rs1016536	64021	170753071	A/C	0.13	0.09	0.173
rs2235506	65685	170754735	C/T			
rs2076998	70220	170759270	A/G			
rs2076997	70323	170759373	A/C	0.92	0.89	0.256
rs2345478	70959	170760009	A/C	0.11	0.10	0.545
rs2021899	73436	170762486	C/G	0.44	0.45	0.797
rs2021898	82945	170771995	A/G			
rs2345682	82958	170772008	G/T			
rs2345683	82961	170772011	C/G	0.23	0.26	0.407
rs2881195	82964	170772014	C/T			
rs2345684	82965	170772015	G/T			
rs3046261	83006	170772056	-/CTTT			
rs4083413	83025	170772075	C/T			
rs4083412	83034	170772084	A/G			
rs2345685	83074	170772124	G/T	0.74	0.71	0.533
rs2021897	83132	170772182	G/T			
rs4036211	83155	170772205	C/T			
rs4036212	83172	170772222	A/T			
rs4036213	83174	170772224	G/T			
rs2345686	83206	170772256	C/T			
rs4036214	83216	170772266	G/T			
rs4036215	83234	170772284	G/T			
rs2345687	83252	170772302	A/G	0.47	0.50	0.457
rs2345688	83260	170772310	A/C	0.61	0.58	0.434
rs2881196	83263	170772313	A/C			
rs3046288	83296	170772346	-/AT			
rs4036216	83319	170772369	A/G			
rs4036205	83322	170772372	C/G			
rs2092307	83324	170772374	A/C			
rs4036206	83357	170772407	C/G			
rs2345689	83375	170772425	C/T			
rs2345690	83381	170772431	C/T			
rs2345691	83389	170772439	A/T			
rs2345692	83443	170772493	A/G			
rs3046306	83499	170772549	-/GGTG			
rs4036207	83545	170772595	C/T			
rs2345693	83566	170772616	C/T			

dbSNP rs#	Position in SEQ ID NO: 1	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2345694	83591	170772641	C/T			
rs2345695	83619	170772669	G/T			
rs2345696	83698	170772748	A/G			
rs4036209	83780	170772830	G/T			
rs2345697	83784	170772834	G/T			
rs2881197	83826	170772876	G/T			
rs2345698	83832	170772882	C/T			
rs2345699	83852	170772902	C/T			
rs2744640	86297	170775347	C/T	0.57	0.55	0.595
rs2744639	86315	170775365	G/T	0.35	0.34	0.752
rs2744638	86420	170775470	C/G	0.41	0.40	0.793
rs2744637	86460	170775510	C/G	0.47	0.46	0.836
rs2744636	86714	170775764	C/T	0.83	NA	
rs2744635	86718	170775768	C/T			
rs2744634	86736	170775786	C/G	untyped	0.97	NA
rs2744633	86753	170775803	C/T	0.09	0.10	0.691
rs2744632	86766	170775816	G/T	0.74	0.72	0.529
rs2744630	88162	170777212	C/G			
rs2744629	88218	170777268	A/G	0.81	0.81	0.959
rs2744628	88246	170777296	A/G	0.74	NA	
rs2744627	88255	170777305	C/T	0.33	0.29	0.341
rs2977616	88309	170777359	G/T			
rs2977617	88310	170777360	A/T			
rs2744626	88471	170777521	A/G			
rs2744625	88619	170777669	C/T			
rs3115847	88904	170777954	C/T			
rs2744623	89044	170778094	C/G			
rs4036193	90531	170779581	-/AAAAA			
rs4036194	90534	170779584	A/G			
rs4036196	90613	170779663	C/G			
rs1042327	46252	170735302	C/T	0.42	0.43	0.880

[0233] Allelotyping results were considered particularly significant with a calculated p-value of less than or equal to 0.05 for allelotype results. These values are indicated in bold. The allelotyping p-values were plotted in Figure 1A for the discovery cohort. The position of each SNP on the chromosome is presented on the x-axis. The y-axis gives the negative logarithm (base 10) of the p-value comparing the estimated allele in the case group to that of the control group. The minor allele frequency of the control group for each SNP designated by an X or other symbol on the graphs in Figure 1A can be determined by consulting Table 13. For example, the left-most X on the left graph is at position 170689279. By proceeding down the Table from top to bottom and across the graphs from left to right the allele frequency associated with each symbol shown can be determined.

[0234] To aid the interpretation, multiple lines have been added to the graph. The broken horizontal lines are drawn at two common significance levels, 0.05 and 0.01. The vertical broken lines are drawn every 20kb to assist in the interpretation of distances between SNPs. Two other lines are drawn to expose linear trends in the association of SNPs to the disease. The light gray line (or generally bottom-most curve) is a nonlinear smoother through the data points on the graph using a local polynomial

regression method (W.S. Cleveland, E. Grosse and W.M. Shyu (1992) Local regression models. Chapter 8 of Statistical Models in S eds J.M. Chambers and T.J. Hastie, Wadsworth & Brooks/Cole.). The black line provides a local test for excess statistical significance to identify regions of association. This was created by use of a 10kb sliding window with 1kb step sizes. Within each window, a chi-square goodness of fit test was applied to compare the proportion of SNPs that were significant at a test wise level of 0.01, to the proportion that would be expected by chance alone (0.05 for the methods used here). Resulting p-values that were less than 10^{-8} were truncated at that value.

[0235] Finally, the exons and introns of the genes in the covered region are plotted below each graph at the appropriate chromosomal positions. The gene boundary is indicated by the broken horizontal line. The exon positions are shown as thick, unbroken bars. An arrow is place at the 3' end of each gene to show the direction of transcription.

Example 5

ELP3 Region Proximal SNPs

[0236] It has been discovered that SNP rs1563055 in elongation protein 3 homolog (*ELP3*) is associated with occurrence of osteoarthritis in subjects.

[0237] Thirty-three additional allelic variants proximal to rs1563055 were identified and subsequently allelotyped in osteoarthritis case and control sample sets as described in Examples 1 and 2. The polymorphic variants are set forth in Table 16. The chromosome positions provided in column four of Table 16 are based on Genome "Build 34" of NCBI's GenBank.

TABLE 16

dbSNP rs#	Chromosome	Position in SEQ ID NO: 2	Chromosome Position	Allele Variants
rs1000658	8	211	27927511	c/t
rs1984880	8	473	27927773	c/t
rs999112	8	1536	27928836	c/t
rs735880	8	5639	27932939	c/t
rs2045029	8	17186	27944486	a/g
rs2045028	8	17335	27944635	c/t
rs1947384	8	25029	27952329	c/g
rs1947385	8	25111	27952411	c/t
rs1901744	8	28811	27956111	a/g
rs1901745	8	28863	27956163	a/t
rs971882	8	30809	27958109	a/c
rs1377338	8	40985	27968285	a/c
rs2305452	8	45147	27972447	c/t
rs2305451	8	45282	27972582	a/g
rs2123472	8	46168	27973468	g/t
rs2167768	8	46328	27973628	a/g

dbSNP rs#	Chromosome	Position in SEQ ID NO: 2	Chromosome Position	Allele Variants
rs1563055	8	49077	27976377	a/g
rs2290371	8	51925	27979225	c/t
rs2290370	8	52141	27979441	a/g
rs2290369	8	52168	27979468	c/t
rs2874904	8	60852	27988152	c/t
rs3213997	8	62468	27989768	a/g
rs3213998	8	65572	27992872	g/t
rs1530929	8	79089	28006389	a/c
rs1000275	8	79541	28006841	c/t
rs1000274	8	79790	28007090	c/t
rs3757896	8	90843	28018143	a/g
rs3757895	8	90978	28018278	c/t
rs3757894	8	91052	28018352	c/g
rs3757893	8	91131	28018431	a/g
rs3757892	8	91132	28018432	c/t
rs3757891	8	94439	28021739	a/g
rs3757890	8	94621	28021921	a/t

Assay for Verifying and Allelotyping SNPs

[0238] The methods used to verify and allelotype the 33 proximal SNPs of Table 16 are the same methods described in Examples 1 and 2 herein. The primers and probes used in these assays are provided in Table 17 and Table 18, respectively.

TABLE 17

dbSNP rs#	Forward PCR primer	Reverse PCR primer
Rs1000658	ACGTTGGATGTTCTCAAAAAAGAAACACAT	ACGTTGGATGGGGTTATCAGTTTGAGATTC
Rs1984880	ACGTTGGATGCCATTTGCCAATTCCTGTGG	ACGTTGGATGATGGGCTGAAATGTATCCCC
rs999112	ACGTTGGATGCTAAGCACATGCCTTTCTTG	ACGTTGGATGCTATTTTCTACTGGGAGATG
rs735880	ACGTTGGATGTGCCTTCATTCTCCAACCAC	ACGTTGGATGAACAGAGTGAGACCCATCTG
Rs2045029	ACGTTGGATGAGTCATTGCTAGCTTTCTGG	ACGTTGGATGGGGACTTTAGGGAAGTTATAG
Rs2045028	ACGTTGGATGAGCTTGTAGTGAGCCGAGAT	ACGTTGGATGTGAGACAGAGTCTTGCTCTG
Rs1947384	ACGTTGGATGATTCTCCACCGAGAAACCAG	ACGTTGGATGTTGTGGCAGCAAGAAGGAAC
Rs1947385	ACGTTGGATGAAATTTCAACAGTCAACAAT	ACGTTGGATGGTCAGTTTTGAAAACTGATC
Rs1901744	ACGTTGGATGCCTTGATTGAAGAGTAAAGC	ACGTTGGATGATCAAATATTCCTCATCCCC
Rs1901745	ACGTTGGATGCTTCTGCCTTTACCTGTGTC	ACGTTGGATGAAATGAAGCAGCACTCACAG
rs971882	ACGTTGGATGAAGCCCTAATCATTGGTACG	ACGTTGGATGGATGGGTGCTAAAAAGACAC
Rs1377338	ACGTTGGATGCCCACATATCTACACATCAAG	ACGTTGGATGAGGGAGATAGGTGGTTAAAG
Rs2305452	ACGTTGGATGCCGTGTTGCAACTAACAGGG	ACGTTGGATGAGACGTTCCCATCCTCCATC
Rs2305451	ACGTTGGATGGCAGAGCCACCAGAGATAAA	ACGTTGGATGTTTTACGACAGGCGGGATTG
Rs2123472	ACGTTGGATGCACTTAGAATTGTTGCTTGG	ACGTTGGATGGCTGTATCTGTGACCTCAAA
Rs2167768	ACGTTGGATGGAATCAACATGACTTGGTGAC	ACGTTGGATGATCTCACTCTAACTTGCTCC
rs1563055	ACGTTGGATGAGTTCTTTCTCCTCACATTG	ACGTTGGATGCCCTTTAGAAGCACATACTC
Rs2290371	ACGTTGGATGATCCTCTTGGTAGCTTGTCC	ACGTTGGATGCTGTCTTGGTTTTCACCCTG

dbSNP rs#	Forward PCR primer	Reverse PCR primer
Rs2290370	ACGTTGGATGCAACCTCTACCTCACTACAC	ACGTTGGATGATGAGGTATCGACACACTGG
Rs2290369	ACGTTGGATGACACACTGGGTATCTGTTCT	ACGTTGGATGTCAGAATCCCCAACCTCTAC
Rs2874904	ACGTTGGATGAAATTCCAGGCTGGGTACAG	ACGTTGGATGTGCTGACCTTAAGTGATCCG
Rs3213997	ACGTTGGATGGGTTGGCTAGAAGAGAAAAA	ACGTTGGATGTACAGTCCTTTTGAAACTAC
Rs3213998	ACGTTGGATGACAGTTTGTTGACATAGTAG	ACGTTGGATGAGGCTGAAAAGACATTCATG
Rs1530929	ACGTTGGATGGGCTTTCACTATATTTCCTC	ACGTTGGATGGAATACAGTAAGCCTATGGG
Rs1000275	ACGTTGGATGAACCCCAGAAAGCAAAAAGC	ACGTTGGATGCACGCTTGCTAACTTAATGG
Rs1000274	ACGTTGGATGGCCTAAGACAGGATCCAAAC	ACGTTGGATGTTACTGCGTGCCTTAGTACC
Rs3757896	ACGTTGGATGCCTTCAAGCAAGTCAGTTAC	ACGTTGGATGCAGAAACTGTGTGACTGATC
Rs3757895	ACGTTGGATGAAAATCATTGGCCAAACTGC	ACGTTGGATGCTCCTTAGTATTCTTAGGTG
Rs3757894	ACGTTGGATGAGAAGGGTTGAACAACAAGG	ACGTTGGATGCACCTAAGAATACTAAGGAG
Rs3757893	ACGTTGGATGCCCTTGTTGTTCAACCCTTC	ACGTTGGATGCTGCATGTGGATACCTACAC
Rs3757892	ACGTTGGATGTCCTGCATGTGGATACCTAC	ACGTTGGATGCCCTTGTTGTTCAACCCTTC
Rs3757891	ACGTTGGATGATGGGCCAATTCTCCATAGG	ACGTTGGATGAGGCCTGTTAAGGAAACCTG
Rs3757890	ACGTTGGATGCAGGTGGATGTAGGCTTAAG	ACGTTGGATGGCACCACTGCCTCTTGTTTT

TABLE 18

dbSNP rs#	Extend Primer	Term Mix
rs1000658	AATTGACAATGTTGGGACTGTT	ACG
rs1984880	TGTGGTGTAAATAGGAGTTAGTGG	ACT
rs999112	GCACATGCCTTTCTTGGAACTG	ACG
rs735880	AACCTTTACTTGTACTACATGC	ACG
rs2045029	GCTAGCTTTCTGGTAATGAAAAT	ACT
rs2045028	GATCGCACCACTGCACTCCAG	ACG
rs1947384	ATAGCGGCAGTCCAAAAAGC	ACT
rs1947385	TTCAACAGTCAACAATGAAACC	ACT
rs1901744	ATAGTCAAGTATGCAAATGAAGC	ACT
rs1901745	CCTTTACCTGTGTCTTCCCT	CGT
rs971882	CCTAATCATTGGTACGGTCTCA	ACT
rs1377338	AGTATTAGCTCAAATATCACATTG	ACT
rs2305452	CAGGGTAGCAGGCGGCC	ACG
rs2305451	CCACAAACTCAGACCACGG	ACT
rs2123472	CAGTTAATGTCAAGAAGCATAG	ACT
rs2167768	ACATGACTTGGTGACAGAAGAA	ACT
rs1563055	TTCTCCTCACATTGTTTCTACT	ACG
rs2290371	GGTAGCTTGTCCTTAAATAACCGT	ACT
rs2290370	GGAGCAGGGACTTCTGCCA	ACT
rs2290369	AGTCCCTGCTCCATGTGAC	ACT
rs2874904	GGCTAACGCCTGTAATCCCA	ACT
rs3213997	AGAAAAATATTGTTATGCCCACA	ACG
rs3213998	TAGTATTCTCAAATAGAGAGATTC	ACT
rs1530929	TTTCCTCTTTCCAGAATTGTATTT	ACT
rs1000275	ATGAGAATATCCTAGAATGAGGCA	ACG

dbSNP rs#	Extend Primer	Term Mix
rs1000274	GAATCATCAGGTCCTGTGCC	ACG
rs3757896	TAATTCTCCTTAAGTAGTTAATTC	ACT
rs3757895	TTGGCCAAACTGCAGGATCT	ACT
rs3757894	AAGGGCCACACAAGCAATTTCAA	ACT
rs3757893	CCAAAGGACATTAGGTGGTG	ACG
rs3757892	TGTGGATACCTACACTGCTC	ACG
rs3757891	AGGATAAGTGTAACGGGGTC	ACT
rs3757890	AGTGACACTCTTACTTCACAC	CGT

Genetic Analysis

[0239] Allelotyping results from the discovery cohort are shown for cases and controls in Table 19. The allele frequency for the A2 allele is noted in the fifth and sixth columns for osteoarthritis case pools and control pools, respectively, where "AF" is allele frequency. The allele frequency for the A1 allele can be easily calculated by subtracting the A2 allele frequency from 1 (A1 AF = 1-A2 AF). For example, the SNP rs1000658 has the following case and control allele frequencies: case A1 (C) = 0.36; case A2 (T) = 0.64; control A1 (C) = 0.37; and control A2 (T) = 0.63, where the nucleotide is provided in paranthesis. Some SNPs are labeled "untyped" because of failed assays.

TABLE 19

dbSNP rs#	Position in SEQ ID NO: 2	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
Rs1000658	211	27927511	C/T	0.79	0.80	0.591
Rs1984880	473	27927773	C/T	0.47	0.48	0.735
Rs999112	1536	27928836	C/T	0.72	0.72	0.775
Rs735880	5639	27932939	C/T	0.20	0.19	0.561
Rs2045029	17186	27944486	A/G	0.54	0.56	0.361
Rs2045028	17335	27944635	C/T			
Rs1947384	25029	27952329	C/G	0.63	0.60	0.122
Rs1947385	25111	27952411	C/T			
Rs1901744	28811	27956111	A/G	0.18	0.18	0.796
Rs1901745	28863	27956163	A/T	0.14	0.18	0.117
Rs971882	30809	27958109	A/C			
Rs1377338	40985	27968285	A/C	0.28	0.24	0.085
Rs2305452	45147	27972447	C/T	0.31	0.27	0.078
Rs2305451	45282	27972582	A/G	0.48	0.52	0.130
Rs2123472	46168	27973468	G/T	0.42	0.45	0.239
Rs2167768	46328	27973628	A/G	0.38	0.35	0.350
Rs1563055	49077	27976377	A/G			
Rs2290371	51925	27979225	C/T	0.28	0.24	**0.039**
Rs2290370	52141	27979441	A/G	0.85	0.84	0.551
Rs2290369	52168	27979468	C/T	0.43	0.47	0.138
Rs2874904	60852	27988152	C/T	0.26	0.23	0.132
Rs3213997	62468	27989768	A/G	0.44	0.47	0.201
Rs3213998	65572	27992872	G/T	0.83	0.80	0.223
Rs1530929	79089	28006389	A/C	0.47	0.49	0.556

dbSNP rs#	Position in SEQ ID NO: 2	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
Rs1000275	79541	28006841	C/T	0.86	0.87	0.771
Rs1000274	79790	28007090	C/T	0.54	0.56	0.510
Rs3757896	90843	28018143	A/G			
Rs3757895	90978	28018278	C/T	0.46	0.47	0.874
Rs3757894	91052	28018352	C/G	0.08	0.09	0.709
Rs3757893	91131	28018431	A/G	0.16	0.15	0.590
Rs3757892	91132	28018432	C/T	0.09	0.08	0.595
Rs3757891	94439	28021739	A/G			
Rs3757890	94621	28021921	A/T	0.98	0.96	0.167

[0240] The *ELP3* proximal SNPs were also allelotyped in the replication cohorts using the methods described herein and the primers provided in Tables 17 and 18. The replication allelotyping results for replication cohort #1 and replication cohort #2 are provided in Tables 20 and 21, respectively.

TABLE 20

dbSNP rs#	Position in SEQ ID NO: 2	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1000658	211	27927511	C/T	0.78	0.79	0.863
rs1984880	473	27927773	C/T	0.46	0.48	0.594
rs999112	1536	27928836	C/T	0.71	0.70	0.759
rs735880	5639	27932939	C/T	0.20	0.17	0.255
rs2045029	17186	27944486	A/G	0.55	0.57	0.526
rs2045028	17335	27944635	C/T			
rs1947384	25029	27952329	C/G	0.65	0.61	0.198
rs1947385	25111	27952411	C/T			
rs1901744	28811	27956111	A/G	0.19	0.18	0.674
rs1901745	28863	27956163	A/T	0.15	0.18	0.448
rs971882	30809	27958109	A/C			
rs1377338	40985	27968285	A/C	0.29	0.22	**0.039**
rs2305452	45147	27972447	C/T	0.31	0.26	0.067
rs2305451	45282	27972582	A/G	0.49	0.56	0.063
rs2123472	46168	27973468	G/T	0.42	0.49	**0.039**
rs2167768	46328	27973628	A/G	0.36	0.34	0.396
rs1563055	49077	27976377	A/G			
rs2290371	51925	27979225	C/T	0.28	0.23	0.054
rs2290370	52141	27979441	A/G	0.85	0.83	0.488
rs2290369	52168	27979468	C/T	0.41	0.49	**0.036**
rs2874904	60852	27988152	C/T	0.29	0.22	0.062
rs3213997	62468	27989768	A/G	0.44	0.50	0.064
rs3213998	65572	27992872	G/T	0.84	0.82	0.336
rs1530929	79089	28006389	A/C	0.48	0.52	0.311
rs1000275	79541	28006841	C/T	0.86	0.87	0.566
rs1000274	79790	28007090	C/T	0.54	0.59	0.159
rs3757896	90843	28018143	A/G			
rs3757895	90978	28018278	C/T	0.45	0.49	0.308
rs3757894	91052	28018352	C/G	0.09	0.09	0.914
rs3757893	91131	28018431	A/G	0.15	0.14	0.803
rs3757892	91132	28018432	C/T	0.09	0.08	0.798
rs3757891	94439	28021739	A/G			
rs3757890	94621	28021921	A/T	0.98	0.95	0.159

TABLE 21

dbSNP rs#	Position in SEQ ID NO: 2	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1000658	211	27927511	C/T	0.80	0.82	0.443
rs1984880	473	27927773	C/T	0.48	0.47	0.898
rs999112	1536	27928836	C/T	0.72	0.76	0.319
rs735880	5639	27932939	C/T	0.20	0.22	0.598
rs2045029	17186	27944486	A/G	0.52	0.54	0.581
rs2045028	17335	27944635	C/T			
rs1947384	25029	27952329	C/G	0.62	0.59	0.348
rs1947385	25111	27952411	C/T			
rs1901744	28811	27956111	A/G	0.18	0.18	0.928
rs1901745	28863	27956163	A/T	0.13	0.17	0.113
rs971882	30809	27958109	A/C			
rs1377338	40985	27968285	A/C	0.27	0.27	0.961
rs2305452	45147	27972447	C/T	0.32	0.30	0.673
rs2305451	45282	27972582	A/G	0.47	0.47	0.911
rs2123472	46168	27973468	G/T	0.41	0.38	0.348
rs2167768	46328	27973628	A/G	0.39	0.37	0.664
rs1563055	49077	27976377	A/G			
rs2290371	51925	27979225	C/T	0.28	0.25	0.403
rs2290370	52141	27979441	A/G	0.85	0.84	0.939
rs2290369	52168	27979468	C/T	0.46	0.44	0.712
rs2874904	60852	27988152	C/T	0.24	0.24	0.888
rs3213997	62468	27989768	A/G	0.45	0.43	0.752
rs3213998	65572	27992872	G/T	0.81	0.78	0.373
rs1530929	79089	28006389	A/C	0.46	0.43	0.445
rs1000275	79541	28006841	C/T	0.87	0.86	0.767
rs1000274	79790	28007090	C/T	0.54	0.51	0.394
rs3757896	90843	28018143	A/G			
rs3757895	90978	28018278	C/T	0.47	0.42	0.202
rs3757894	91052	28018352	C/G	0.07	0.09	0.478
rs3757893	91131	28018431	A/G	0.17	0.16	0.653
rs3757892	91132	28018432	C/T	0.09	0.07	0.567
rs3757891	94439	28021739	A/G			
rs3757890	94621	28021921	A/T	0.97	0.97	0.728

[0241] Allelotyping results were considered particularly significant with a calculated p-value of less than or equal to 0.05 for allelotype results. These values are indicated in bold. The allelotyping p-values were plotted in Figure 1B for the discovery cohort. The position of each SNP on the chromosome is presented on the x-axis. The y-axis gives the negative logarithm (base 10) of the p-value comparing the estimated allele in the case group to that of the control group. The minor allele frequency of the control group for each SNP designated by an X or other symbol on the graphs in Figure 1B can be determined by consulting Table 19. For example, the left-most X on the left graph is at position 27927511. By proceeding down the Table from top to bottom and across the graphs from left to right the allele frequency associated with each symbol shown can be determined.

[0242] To aid the interpretation, multiple lines have been added to the graph. The broken horizontal lines are drawn at two common significance levels, 0.05 and 0.01. The vertical broken lines are drawn every 20kb to assist in the interpretation of distances between SNPs. Two other lines are drawn to

expose linear trends in the association of SNPs to the disease. The light gray line (or generally bottom-most curve) is a nonlinear smoother through the data points on the graph using a local polynomial regression method (W.S. Cleveland, E. Grosse and W.M. Shyu (1992) Local regression models. Chapter 8 of Statistical Models in S eds J.M. Chambers and T.J. Hastie, Wadsworth & Brooks/Cole.). The black line provides a local test for excess statistical significance to identify regions of association. This was created by use of a 10kb sliding window with 1kb step sizes. Within each window, a chi-square goodness of fit test was applied to compare the proportion of SNPs that were significant at a test wise level of 0.01, to the proportion that would be expected by chance alone (0.05 for the methods used here). Resulting p-values that were less than 10^{-8} were truncated at that value.

[0243] Finally, the exons and introns of the genes in the covered region are plotted below each graph at the appropriate chromosomal positions. The gene boundary is indicated by the broken horizontal line. The exon positions are shown as thick, unbroken bars. An arrow is place at the 3' end of each gene to show the direction of transcription.

Example 6

CHDC1 Region Proximal SNPs

[0244] It has been discovered that SNP rs912428 in calponin homology (CH) domain containing 1 (*CHDC1*) is associated with occurrence of osteoarthritis in subjects.

[0245] Forty-three additional allelic variants proximal to rs912428 were identified and subsequently allelotyped in osteoarthritis case and control sample sets as described in Examples 1 and 2. The polymorphic variants are set forth in Table 22. The chromosome positions provided in column four of Table 22 are based on Genome "Build 34" of NCBI's GenBank.

TABLE 22

dbSNP rs#	Chromosome	Position in SEQ ID NO: 3	Chromosome Position	Allele Variants
rs1012628	13	243	44917643	c/t
rs1570976	13	10208	44927608	c/t
rs912436	13	15049	44932449	c/t
rs912435	13	15111	44932511	a/g
rs912433	13	15272	44932672	c/t
rs912432	13	15287	44932687	a/g
rs912431	13	15326	44932726	a/g
rs912430	13	15327	44932727	c/t
rs1408225	13	17038	44934438	c/t
rs998657	13	19391	44936791	a/g
rs1324006	13	21702	44939102	c/t
rs1924417	13	22431	44939831	c/g
rs2038728	13	22881	44940281	a/g

dbSNP rs#	Chromosome	Position in SEQ ID NO: 3	Chromosome Position	Allele Variants
rs912429	13	27744	44945144	a/t
rs3742269	13	32564	44949964	a/g
rs3742270	13	32698	44950098	a/c
rs3803192	13	33104	44950504	g/t
rs3803191	13	33181	44950581	c/t
rs754106	13	33256	44950656	c/t
rs2005053	13	33543	44950943	c/t
rs1535793	13	35567	44952967	c/t
rs1886220	13	40085	44957485	c/t
rs1886219	13	40482	44957882	a/t
rs1535792	13	45641	44963041	a/t
rs1535791	13	46059	44963459	a/g
rs912428	13	48504	44965904	c/t
rs1886218	13	48919	44966319	a/c
rs1570622	13	49693	44967093	c/t
rs912427	13	49874	44967274	a/g
rs912426	13	50020	44967420	a/g
rs3068693	13	50616	44968016	-/ttt
rs1570621	13	50719	44968119	a/g
rs1886965	13	55511	44972911	c/t
rs1008849	13	65533	44982933	a/g
rs912434	13	70529	44987929	a/c
rs3889095	13	75591	44992991	c/t
rs716223	13	77266	44994666	g/t
rs2897207	13	80368	44997768	g/t
rs1570620	13	82475	44999875	a/g
rs1467605	13	92462	45009862	g/t
rs1467604	13	92480	45009880	c/t
rs1408224	13	95819	45013219	c/t
rs1408223	13	96275	45013675	c/t

Assay for Verifying and Allelotyping SNPs

[0246] The methods used to verify and allelotype the 43 proximal SNPs of Table 22 are the same methods described in Examples 1 and 2 herein. The primers and probes used in these assays are provided in Table 23 and Table 24, respectively.

TABLE 23

dbSNP rs#	Forward PCR primer	Reverse PCR primer
Rs1012628	ACGTTGGATGGATTTTCTGTGTCCCCCAAG	ACGTTGGATGTTGCAACAGAGAGAGCTCTG
Rs1570976	ACGTTGGATGTGATGTGTCTGCTGTGTTGG	ACGTTGGATGTTCACATGGCGAGGTCTTAG
rs912436	ACGTTGGATGCCATATAAGGTGGTTATGGG	ACGTTGGATGCAAACAGGTTTTTCTGAGGC
rs912435	ACGTTGGATGCAAGCCAATATCCAAGACAG	ACGTTGGATGAAAAACCTGTTTGTGAGGCC

dbSNP rs#	Forward PCR primer	Reverse PCR primer
rs912433	ACGTTGGATGTGCCTTCCATCCTTAACACG	ACGTTGGATGGGCTTGAGCTTAGATATGGC
rs912432	ACGTTGGATGAAATAGTTGGGTTTTGTGCC	ACGTTGGATGATTTGGTGTTAATTGCAGTG
rs912431	ACGTTGGATGTGGAAGGCACAAAACCCAAC	ACGTTGGATGCAGAAGCTAGGCTTCCTATG
rs912430	ACGTTGGATGTGGAAGGCACAAAACCCAAC	ACGTTGGATGCAGAAGCTAGGCTTCCTATG
Rs1408225	ACGTTGGATGGGGCACCATGACAATATTCC	ACGTTGGATGACACCTTGATCTTGGACTTC
rs998657	ACGTTGGATGACTGGGCCAGGGAGGAATAG	ACGTTGGATGGTTGGGGAGATAATACAGAAG
Rs1324006	ACGTTGGATGGCTGAAAACCCAAATGTGTG	ACGTTGGATGCCAGCTATCAGCTCCATTTC
Rs1924417	ACGTTGGATGACAAAAGCAAGCCTTCACAG	ACGTTGGATGGTACTGTAAAAGGTACTGTG
Rs2038728	ACGTTGGATGAAGGCTTTTGGACACAAGTC	ACGTTGGATGGCACCTCTTATGATGTTCCC
rs912429	ACGTTGGATGTTCAATTCCCCAAAGCCCTC	ACGTTGGATGGGCAAGTTCCATAACCTCTC
Rs3742269	ACGTTGGATGGAGAAAAGAGAACGAGAAGG	ACGTTGGATGTAAATGACAGCAGTCTGGAG
Rs3742270	ACGTTGGATGCTAAAACCAAAGCTGACGGG	ACGTTGGATGTTCTGCTCCTGTGGCATAGC
Rs3803192	ACGTTGGATGTCCTTTTGCTTCTGCGATGC	ACGTTGGATGTGCTTCCCCATCAGTTCTTG
Rs3803191	ACGTTGGATGCTGTCTGTACATTACCAGGC	ACGTTGGATGAATAGCAGCTGGAGGATCTC
rs754106	ACGTTGGATGTTCTTACCATCCAGCAAGGC	ACGTTGGATGGCCTGGTAATGTACAGACAG
Rs2005053	ACGTTGGATGCTGTTGCTAGCTTGGATTTG	ACGTTGGATGTTCCCTGTCCTTTCTGGCAT
Rs1535793	ACGTTGGATGAACAAAGAGGAACAGAGCCC	ACGTTGGATGGCATAAGCCCCTTTTCCTAG
Rs1886220	ACGTTGGATGTCACCGTGTTAGCGAGAATG	ACGTTGGATGTAATCCCAGCACTTTGGGAG
Rs1886219	ACGTTGGATGTGTAACTGGATTTGCTGGAG	ACGTTGGATGTACATCAATAGCCGAGGAAG
Rs1535792	ACGTTGGATGCTGTATATCAGTGACTGTCC	ACGTTGGATGCAGAGAAGAAACATCTCAGC
Rs1535791	ACGTTGGATGGAGGGTTTATCCTTACAATTG	ACGTTGGATGTTTTAGGGTCCCTTGATAAG
rs912428	ACGTTGGATGACTACATCCATTCCAGGGAG	ACGTTGGATGTCAGATCAGAGTGAGTTTAG
Rs1886218	ACGTTGGATGTCCCGAAAACAAGTCAAGAC	ACGTTGGATGAGTCCAGGCAAAACAGTAAG
Rs1570622	ACGTTGGATGATAGCTGCCACACTCTTTAG	ACGTTGGATGGCGCAGTTTAGAAAAACCTG
rs912427	ACGTTGGATGTAGGGTTCTCGATGGGTATG	ACGTTGGATGTTTGCCCTGGTCACTTTAGG
rs912426	ACGTTGGATGTTAGAGGATGCATAGGCCAG	ACGTTGGATGAAGTCACTTACTGCATGGTC
Rs3068693	ACGTTGGATGAAATTGGCCACATGGAATCC	ACGTTGGATGCTACCTTTAACATCCCTGTC
Rs1570621	ACGTTGGATGAATTAAGAATGGCAGCTATG	ACGTTGGATGGTTTAAAACTAAAAACAC
Rs1886965	ACGTTGGATGCTGCTAAGGATATGTGTTTCC	ACGTTGGATGACACCAGTGCTCAGTATTTG
Rs1008849	ACGTTGGATGGCAGTTGTGAATTGTGCAGC	ACGTTGGATGTGGTGCAGAACATGTCAGAC
rs912434	ACGTTGGATGTTCTGACATGTACAGACGTG	ACGTTGGATGTCCTGGGAAATCTTTCCATC
Rs3889095	ACGTTGGATGAAGGTAATGATATGTCCCCC	ACGTTGGATGCGCATTTTACAGAGACATTG
rs716223	ACGTTGGATGACACTGTCTCTAGAAGCAGG	ACGTTGGATGGAAGCAGGAAAAGAGTGAGG
Rs2897207	ACGTTGGATGTCAGCCTCCAGAACTATGAG	ACGTTGGATGAACAGAGAGAGACCCTGTCT
Rs1570620	ACGTTGGATGCTGTTCCTGCCTTGATATGG	ACGTTGGATGGAAGGAAGTCTATTCAGCCC
Rs1467605	ACGTTGGATGATGTTACAGGGTGGTAAGCG	ACGTTGGATGTAAAGTTGCCACGCTTCTCC
Rs1467604	ACGTTGGATGATATACGGCATGTTACAGGG	ACGTTGGATGTTAAAGTTGCCACGCTTCTC
Rs1408224	ACGTTGGATGACTTCCCACTCCTCTAGACA	ACGTTGGATGTATTGGCTGGGTAGCACTCC
Rs1408223	ACGTTGGATGTCATTACCAGTTCCACAGAG	ACGTTGGATGTTGAGACATCATGAGGAGTG

TABLE 24

dbSNP rs#	Extend Primer	Term Mix
Rs1012628	CTGTGTCCCCCAAGTCTTTG	ACG
Rs1570976	TTGGCATTTCTTTGAGAA	ACT
rs912436	AGGTGGTTATGGGTTTGTCACTCA	ACT
rs912435	TCCAAAAAGCCCAAGAAATTCT	ACT
rs912433	CCTTAACACGTTTATAATAGATTA	ACG
rs912432	GTGCCTTCCATCCTTAACAC	ACT
rs912431	GGCACAAAACCCAACTATTTTTC	ACG
rs912430	GCACAAAACCCAACTATTTTTCC	ACT
Rs1408225	CCTCAGACTGGGTGGCTTA	ACT
rs998657	CACCCACCTGAGGGAGGC	ACT
Rs1324006	GATACCTTGAAGAATTTTTAAAAC	ACG
Rs1924417	TTTAGGCACATTTGTACTTATAAA	ACT
Rs2038728	TGGACACAAGTCCATGCAACA	ACG
rs912429	CTGTGACAGGTGCTATTATCA	CGT
Rs3742269	TTTTGGACCGATTTCCGGTG	ACT
Rs3742270	GCTGACGGGGATTCCCTTTA	ACT
Rs3803192	GATGCACTAAAAGCAGCAATGT	ACT
Rs3803191	TCCAGCCTTCATATTTTCCTC	ACG
rs754106	ATCCAGCAAGGCACTTAGAAT	ACT
Rs2005053	TGTGGCCTTCAGATGCTTACAT	ACG
Rs1535793	GAGGAACAGAGCCCAAAGGACA	ACT
Rs1886220	CTGACCTCGTGATCCGCC	ACG
Rs1886219	ACTGGATTTGCTGGAGTTAAGAA	CGT
Rs1535792	TATCAGTGACTGTCCTTTTCTTTT	CGT
Rs1535791	TTATCCTTACAATTGAAGAAAGGA	ACT
rs912428	CCATTCCAGGGAGACTCCCA	ACT
Rs1886218	GAAAACAAGTCAAGACATTTATTG	ACT
Rs1570622	CTGCCACACTCTTTAGATGAAGTT	ACG
rs912427	GGGAGATGACAGAACAAAACT	ACT
rs912426	AGGTGCCAAGTGTTAGAAGAAAC	ACG
Rs3068693	GCCTCACATTGTTTTTTTTTTTTT	ACT
Rs1570621	TCGGTCATAACTTTAATGAAGG	ACG
Rs1886965	TGATTTTATGACTCACATTATTTC	ACT
Rs1008849	GTGAATTGTGCAGCTATAAACATG	ACG
rs912434	AGACGTGCCCAGCTATGATA	ACT
Rs3889095	TCCCCCATAACATTTCAGCAT	ACT
rs716223	GTGGTTTGTATTTCCAGTGTCA	ACT
Rs2897207	AACTATGAGAAATAAATGTGTGGG	ACT
Rs1570620	TTGATATGGTTCTTGGTTGTTGG	ACG
Rs1467605	GTAAGCGCTAGAAAGAAAAATAA	ACT
Rs1467604	ACGGCATGTTACAGGGTGGTAAG	ACG
Rs1408224	GGGCACACATTCAGAACTGCCC	ACG
Rs1408223	ACAGAGGAAGACCAAATGACA	ACG

Genetic Analysis

[0247] Allelotyping results from the discovery cohort are shown for cases and controls in Table 25. The allele frequency for the A2 allele is noted in the fifth and sixth columns for osteoarthritis case pools and control pools, respectively, where "AF" is allele frequency. The allele frequency for the A1 allele can be easily calculated by subtracting the A2 allele frequency from 1 (A1 AF = 1-A2 AF). For example, the SNP rs1570976 has the following case and control allele frequencies: case A1 (C) = 0.49; case A2 (T) = 0.51; control A1 (C) = 0.53; and control A2 (T) = 0.47, where the nucleotide is provided in paranthesis. Some SNPs are labeled "untyped" because of failed assays.

TABLE 25

dbSNP rs#	Position in SEQ ID NO: 3	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1012628	243	44917643	C/T	0.70	0.70	0.768
rs1570976	10208	44927608	C/T	0.51	0.47	0.125
rs912436	15049	44932449	C/T	0.98	untpyed	
rs912435	15111	44932511	A/G	0.64	0.36	**~0.0001**
rs912433	15272	44932672	C/T	0.22	0.23	0.581
rs912432	15287	44932687	A/G	0.46	0.44	0.282
rs912431	15326	44932726	A/G	0.46	0.46	0.969
rs912430	15327	44932727	C/T	0.20	0.19	0.584
rs1408225	17038	44934438	C/T			
rs998657	19391	44936791	A/G	0.47	0.44	0.254
rs1324006	21702	44939102	C/T	0.55	0.53	0.419
rs1924417	22431	44939831	C/G	0.53	0.49	0.108
rs2038728	22881	44940281	A/G	0.34	0.38	0.082
rs912429	27744	44945144	A/T			
rs3742269	32564	44949964	A/G	0.83	0.83	0.967
rs3742270	32698	44950098	A/C	0.53	0.50	0.170
rs3803192	33104	44950504	G/T			
rs3803191	33181	44950581	C/T			
rs754106	33256	44950656	C/T	0.40	0.41	0.714
rs2005053	33543	44950943	C/T	0.40	0.40	0.877
rs1535793	35567	44952967	C/T	0.26	0.26	0.910
rs1886220	40085	44957485	C/T			
rs1886219	40482	44957882	A/T	0.21	0.22	0.867
rs1535792	45641	44963041	A/T	0.73	0.71	0.550
rs1535791	46059	44963459	A/G	0.08	0.15	**0.009**
rs912428	48504	44965904	C/T			
rs1886218	48919	44966319	A/C			
rs1570622	49693	44967093	C/T	0.73	0.75	0.451
rs912427	49874	44967274	A/G	0.68	0.70	0.352
rs912426	50020	44967420	A/G	0.76	0.77	0.680
rs3068693	50616	44968016	-/TTT	0.22	0.21	0.597
rs1570621	50719	44968119	A/G	0.19	0.18	0.569
rs1886965	55511	44972911	C/T			
rs1008849	65533	44982933	A/G	0.48	0.43	0.160
rs912434	70529	44987929	A/C	0.23	0.23	0.988
rs3889095	75591	44992991	C/T	0.90	0.90	0.880
rs716223	77266	44994666	G/T	0.91	0.90	0.981
rs2897207	80368	44997768	G/T	0.46	0.46	0.921
rs1570620	82475	44999875	A/G	0.67	0.68	0.738
rs1467605	92462	45009862	G/T	0.29	0.22	**0.044**

dbSNP rs#	Position in SEQ ID NO: 3	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1467604	92480	45009880	C/T	0.68	0.67	0.537
rs1408224	95819	45013219	C/T	0.66	0.65	0.683
rs1408223	96275	45013675	C/T	0.29	0.28	0.587

[0248] The *CHDC1* proximal SNPs were also allelotyped in the replication cohorts using the methods described herein and the primers provided in Tables 23 and 24. The replication allelotyping results for replication cohort #1 and replication cohort #2 are provided in Tables 26 and 27, respectively.

TABLE 26

dbSNP rs#	Position in SEQ ID NO: 3	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1012628	243	44917643	C/T	0.69	0.72	0.337
rs1570976	10208	44927608	C/T	0.48	0.46	0.490
rs912436	15049	44932449	C/T			
rs912435	15111	44932511	A/G	0.16	untyped	0.637
rs912433	15272	44932672	C/T	0.28	0.28	0.984
rs912432	15287	44932687	A/G	0.46	0.42	0.260
rs912431	15326	44932726	A/G	0.46	0.48	0.602
rs912430	15327	44932727	C/T	0.18	0.20	0.476
rs1408225	17038	44934438	C/T			
rs998657	19391	44936791	A/G	0.46	0.43	0.380
rs1324006	21702	44939102	C/T	0.54	0.53	0.811
rs1924417	22431	44939831	C/G	0.51	0.49	0.440
rs2038728	22881	44940281	A/G	0.35	0.39	0.181
rs912429	27744	44945144	A/T			
rs3742269	32564	44949964	A/G	0.84	0.85	0.911
rs3742270	32698	44950098	A/C	0.56	0.50	0.090
rs3803192	33104	44950504	G/T			
rs3803191	33181	44950581	C/T			
rs754106	33256	44950656	C/T	0.40	0.40	0.827
rs2005053	33543	44950943	C/T	0.40	0.37	0.328
rs1535793	35567	44952967	C/T	0.27	0.24	0.259
rs1886220	40085	44957485	C/T			
rs1886219	40482	44957882	A/T	0.22	0.19	0.302
rs1535792	45641	44963041	A/T	0.73	0.76	0.435
rs1535791	46059	44963459	A/G	0.08	0.08	0.958
rs912428	48504	44965904	C/T			
rs1886218	48919	44966319	A/C			
rs1570622	49693	44967093	C/T	0.71	0.79	**0.007**
rs912427	49874	44967274	A/G	0.65	0.73	**0.007**
rs912426	50020	44967420	A/G	0.74	0.80	**0.047**
rs3068693	50616	44968016	-/TTT	0.25	0.21	0.236
rs1570621	50719	44968119	A/G	0.22	0.15	**0.028**
rs1886965	55511	44972911	C/T			
rs1008849	65533	44982933	A/G	0.47	untyped	NA
rs912434	70529	44987929	A/C	0.24	0.19	0.083
rs3889095	75591	44992991	C/T	0.91	0.91	0.867
rs716223	77266	44994666	G/T	0.91	0.93	0.598
rs2897207	80368	44997768	G/T	0.48	0.45	0.321
rs1570620	82475	44999875	A/G	0.66	0.72	**0.034**
rs1467605	92462	45009862	G/T	0.29	0.22	**0.044**
rs1467604	92480	45009880	C/T	0.66	0.70	0.307

dbSNP rs#	Position in SEQ ID NO: 3	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1408224	95819	45013219	C/T	0.64	0.67	0.312
rs1408223	96275	45013675	C/T	0.31	0.23	**0.028**

TABLE 27

dbSNP rs#	Position in SEQ ID NO: 3	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1012628	243	44917643	C/T	0.71	0.68	0.438
rs1570976	10208	44927608	C/T	0.55	0.50	0.159
rs912436	15049	44932449	C/T			
rs912435	15111	44932511	A/G	0.66	untyped	
rs912433	15272	44932672	C/T	0.14	0.17	0.479
rs912432	15287	44932687	A/G	0.47	0.46	0.806
rs912431	15326	44932726	A/G	0.46	0.44	0.513
rs912430	15327	44932727	C/T	0.23	0.17	0.084
rs1408225	17038	44934438	C/T			
rs998657	19391	44936791	A/G	0.48	0.45	0.518
rs1324006	21702	44939102	C/T	0.55	0.52	0.324
rs1924417	22431	44939831	C/G	0.54	0.49	0.123
rs2038728	22881	44940281	A/G	0.34	0.37	0.295
rs912429	27744	44945144	A/T			
rs3742269	32564	44949964	A/G	0.82	0.82	0.861
rs3742270	32698	44950098	A/C	0.50	0.49	0.873
rs3803192	33104	44950504	G/T			
rs3803191	33181	44950581	C/T			
rs754106	33256	44950656	C/T	0.41	0.44	0.346
rs2005053	33543	44950943	C/T	0.40	0.44	0.302
rs1535793	35567	44952967	C/T	0.25	0.31	0.096
rs1886220	40085	44957485	C/T			
rs1886219	40482	44957882	A/T	0.20	0.27	0.053
rs1535792	45641	44963041	A/T	0.73	0.63	**0.007**
rs1535791	46059	44963459	A/G	NA	0.27	NA
rs912428	48504	44965904	C/T			
rs1886218	48919	44966319	A/C			
rs1570622	49693	44967093	C/T	0.75	0.67	**0.040**
rs912427	49874	44967274	A/G	0.71	0.64	0.059
rs912426	50020	44967420	A/G	0.78	0.72	0.065
rs3068693	50616	44968016	-/TTT	0.19	0.21	0.520
rs1570621	50719	44968119	A/G	0.15	0.21	0.077
rs1886965	55511	44972911	C/T			
rs1008849	65533	44982933	A/G	0.49	0.43	0.138
rs912434	70529	44987929	A/C	0.21	0.28	**0.027**
rs3889095	75591	44992991	C/T	0.89	0.88	0.583
rs716223	77266	44994666	G/T	0.90	0.87	0.368
rs2897207	80368	44997768	G/T	0.44	0.48	0.276
rs1570620	82475	44999875	A/G	0.70	0.62	**0.026**
rs1467605	92462	45009862	G/T			
rs1467604	92480	45009880	C/T	0.71	0.62	**0.018**
rs1408224	95819	45013219	C/T	0.68	0.61	0.060
rs1408223	96275	45013675	C/T	0.27	0.34	**0.023**

[0249] Allelotyping results were considered particularly significant with a calculated p-value of less than or equal to 0.05 for allelotype results. These values are indicated in bold. The allelotyping p-values

were plotted in Figure 1C for the discovery cohort. The position of each SNP on the chromosome is presented on the x-axis. The y-axis gives the negative logarithm (base 10) of the p-value comparing the estimated allele in the case group to that of the control group. The minor allele frequency of the control group for each SNP designated by an X or other symbol on the graphs in Figure 1C can be determined by consulting Table 25. For example, the left-most X on the left graph is at position 44917643. By proceeding down the Table from top to bottom and across the graphs from left to right the allele frequency associated with each symbol shown can be determined.

[0250] To aid the interpretation, multiple lines have been added to the graph. The broken horizontal lines are drawn at two common significance levels, 0.05 and 0.01. The vertical broken lines are drawn every 20kb to assist in the interpretation of distances between SNPs. Two other lines are drawn to expose linear trends in the association of SNPs to the disease. The light gray line (or generally bottom-most curve) is a nonlinear smoother through the data points on the graph using a local polynomial regression method (W.S. Cleveland, E. Grosse and W.M. Shyu (1992) Local regression models. Chapter 8 of Statistical Models in S eds J.M. Chambers and T.J. Hastie, Wadsworth & Brooks/Cole.). The black line provides a local test for excess statistical significance to identify regions of association. This was created by use of a 10kb sliding window with 1kb step sizes. Within each window, a chi-square goodness of fit test was applied to compare the proportion of SNPs that were significant at a test wise level of 0.01, to the proportion that would be expected by chance alone (0.05 for the methods used here). Resulting p-values that were less than 10^{-8} were truncated at that value.

[0251] Finally, the exons and introns of the genes in the covered region are plotted below each graph at the appropriate chromosomal positions. The gene boundary is indicated by the broken horizontal line. The exon positions are shown as thick, unbroken bars. An arrow is place at the 3' end of each gene to show the direction of transcription.

Example 7

ERG Region Proximal SNPs

[0252] It has been discovered that SNP rs1888475 in v-ets erythroblastosis virus E26 oncogene like (*ERG)* is associated with occurrence of osteoarthritis in subjects. One hundred sixty-six additional allelic variants proximal to rs1888475 were identified and subsequently allelotyped in osteoarthritis case and control sample sets as described in Examples 1 and 2. The polymorphic variants are set forth in Table 28. The chromosome positions provided in column four of Table 28 are based on Genome "Build 34" of NCBI's GenBank.

TABLE 28

dbSNP rs#	Chromosome	Position in SEQ ID NO: 4	Chromosome Position	Allele Variants
rs2898353	21	231	38783681	a/t
rs960818	21	882	38784332	a/g
rs960819	21	960	38784410	a/c
rs2410034	21	1194	38784644	a/c
rs2836437	21	1530	38784980	a/g
rs2836438	21	1673	38785123	a/g
rs2836439	21	2096	38785546	c/t
rs2836440	21	2285	38785735	a/g
rs2226683	21	5873	38789323	c/t
rs2836441	21	7256	38790706	a/g
rs2836442	21	7988	38791438	a/g
rs2836443	21	8222	38791672	g/t
rs2836444	21	8381	38791831	c/t
rs3787906	21	8814	38792264	c/t
rs3838108	21	8915	38792365	-/c
rs2836445	21	9642	38793092	a/g
rs2836446	21	9902	38793352	a/t
rs3787908	21	10619	38794069	a/g
rs2836447	21	10927	38794377	c/t
rs2836448	21	11032	38794482	c/t
rs2836450	21	14377	38797827	c/t
rs2836451	21	15608	38799058	c/t
rs1015022	21	15928	38799378	c/g
rs2836452	21	16296	38799746	a/g
rs2836453	21	17598	38801048	a/t
rs3787909	21	19272	38802722	a/g
rs2836454	21	20084	38803534	a/g
rs2836455	21	20577	38804027	a/t
rs2155718	21	28051	38811501	a/g
rs2836456	21	29466	38812916	a/g
rs2836457	21	29530	38812980	c/t
rs2836458	21	29987	38813437	a/g
rs2032323	21	30012	38813462	c/t
rs2051400	21	30322	38813772	g/t
rs2836459	21	32216	38815666	c/t
rs2836460	21	32516	38815966	c/t
rs2836461	21	32544	38815994	a/g
rs2836462	21	32746	38816196	a/g
rs2836463	21	33137	38816587	g/t
rs2836464	21	33538	38816988	a/g
rs2836465	21	33798	38817248	c/t
rs2836466	21	33802	38817252	a/c
rs2836467	21	33964	38817414	c/t
rs3827204	21	34132	38817582	a/g
rs2836468	21	34210	38817660	c/t
rs3787911	21	34317	38817767	a/g

dbSNP rs#	Chromosome	Position in SEQ ID NO: 4	Chromosome Position	Allele Variants
rs2836469	21	34499	38817949	c/t
rs2836470	21	34753	38818203	a/c
rs2212599	21	34845	38818295	c/t
rs2836472	21	35335	38818785	c/t
rs2836473	21	36423	38819873	c/t
rs1888469	21	36450	38819900	a/g
rs1888470	21	36481	38819931	g/t
rs2032322	21	38447	38821897	c/g
rs2410035	21	38784	38822234	c/t
rs1573332	21	39387	38822837	a/t
rs2836474	21	39458	38822908	c/t
rs2836475	21	39822	38823272	c/g
rs3787914	21	40305	38823755	c/g
rs1888471	21	40869	38824319	c/t
rs1888472	21	40926	38824376	c/t
rs1888473	21	41010	38824460	c/t
rs1888474	21	41134	38824584	c/t
rs2836476	21	41984	38825434	a/g
rs3787916	21	42172	38825622	a/t
rs2836477	21	42753	38826203	g/t
rs970043	21	43011	38826461	c/t
rs2212600	21	43176	38826626	a/g
rs2836478	21	43320	38826770	g/t
rs2836479	21	43381	38826831	a/t
rs1475877	21	44142	38827592	a/g
rs2836480	21	44383	38827833	a/g
rs2836481	21	44726	38828176	c/t
rs2836483	21	45087	38828537	a/g
rs2836484	21	45141	38828591	c/t
rs2836485	21	45359	38828809	c/g
rs2836486	21	45421	38828871	c/t
rs2836487	21	45456	38828906	c/t
rs1893199	21	45467	38828917	c/t
rs2836488	21	45486	38828936	c/t
rs1893200	21	45709	38829159	a/g
rs1893201	21	45716	38829166	a/g
rs2836489	21	47626	38831076	c/t
rs1888475	21	49413	38832863	a/g
rs2836490	21	49796	38833246	c/t
rs2836491	21	49962	38833412	a/g
rs2836492	21	50075	38833525	c/t
rs2836493	21	50093	38833543	a/g
rs2836494	21	50571	38834021	c/t
rs2836495	21	50615	38834065	a/g
rs2898354	21	50780	38834230	a/g
rs3065390	21	50851	38834301	-/ta
rs2836496	21	51459	38834909	a/c

dbSNP rs#	Chromosome	Position in SEQ ID NO: 4	Chromosome Position	Allele Variants
rs2836497	21	53193	38836643	c/t
rs2836498	21	53702	38837152	c/t
rs2836499	21	53736	38837186	a/c
rs2836500	21	53795	38837245	c/t
rs2836501	21	54109	38837559	a/t
rs2836502	21	54126	38837576	c/t
rs2836503	21	54230	38837680	a/c
rs2836504	21	54894	38838344	c/t
rs3787917	21	55455	38838905	a/g
rs2836505	21	55499	38838949	a/g
rs2836506	21	56522	38839972	c/t
rs2836507	21	56662	38840112	c/t
rs2836508	21	56954	38840404	a/g
rs2836509	21	57267	38840717	a/g
rs2836510	21	58282	38841732	a/g
rs2836511	21	58916	38842366	a/c
rs2212601	21	59544	38842994	c/g
rs2212602	21	59666	38843116	c/t
rs2226682	21	59913	38843363	a/t
rs2836512	21	66846	38850296	a/g
rs2836513	21	67245	38850695	g/t
rs1999328	21	67652	38851102	a/c
rs2212603	21	67955	38851405	a/g
rs3787919	21	67966	38851416	a/c
rs2836514	21	68420	38851870	a/g
rs1023153	21	70226	38853676	a/g
rs1023372	21	70810	38854260	c/t
rs2212604	21	72246	38855696	a/g
rs2226684	21	73330	38856780	g/t
rs2212605	21	73457	38856907	c/t
rs2187307	21	74389	38857839	a/g
rs3065412	21	74638	38858088	-/aa
rs2898355	21	74640	38858090	a/c
rs2836518	21	75358	38858808	a/c
rs3838110	21	75952	38859402	-/g
rs2836519	21	76098	38859548	a/g
rs3827207	21	77836	38861286	a/g
rs2836520	21	78449	38861899	a/c
rs2836521	21	78507	38861957	g/t
rs2836522	21	80031	38863481	g/t
rs2836523	21	81695	38865145	c/t
rs2836524	21	82775	38866225	a/g
rs2836525	21	82795	38866245	a/g
rs3833350	21	84611	38868061	-/c
rs2836526	21	84657	38868107	c/t
rs2836527	21	84693	38868143	a/c
rs3834676	21	85020	38868470	-/t

dbSNP rs#	Chromosome	Position in SEQ ID NO: 4	Chromosome Position	Allele Variants
rs2836528	21	85048	38868498	c/t
rs3761364	21	85100	38868550	c/t
rs2836529	21	85325	38868775	a/c
rs2836530	21	85452	38868902	c/t
rs3761366	21	85868	38869318	a/g
rs2836531	21	85936	38869386	a/g
rs2836532	21	85990	38869440	a/t
rs2836533	21	86139	38869589	c/t
rs2836534	21	86497	38869947	c/t
rs2836535	21	87236	38870686	a/g
rs2836536	21	87248	38870698	c/t
rs3827208	21	87533	38870983	c/g
rs715860	21	87912	38871362	a/g
rs717231	21	88108	38871558	g/t
rs2836537	21	88494	38871944	a/c
rs2836538	21	89598	38873048	a/c
rs2836539	21	90235	38873685	a/t
rs2836540	21	91287	38874737	g/t
rs2836541	21	91359	38874809	c/t
rs2836542	21	92384	38875834	a/c
rs2836543	21	92410	38875860	c/t
rs881837	21	92900	38876350	c/t
rs3949052	21	94495	38877945	a/g
rs2065307	21	94512	38877962	a/g
rs3216105	21	97777	38881227	-/a
rs2073427	21	98333	38881783	c/t

Assay for Verifying and Allelotyping SNPs

[0253] The methods used to verify and allelotype the 166 proximal SNPs of Table 28 are the same methods described in Examples 1 and 2 herein. The primers and probes used in these assays are provided in Table 29 and Table 30, respectively.

TABLE 29

dbSNP rs#	Forward PCR primer	Reverse PCR primer
rs2898353	ACGTTGGATGAATGTGAATGTGGAGGTAGC	ACGTTGGATGCTCCCTTGCTGGTTTTTTTG
rs960818	ACGTTGGATGTGGGATTTTTCCCAGAAGAG	ACGTTGGATGCTGTGCAGAGAAACATGATG
rs960819	ACGTTGGATGCTGTCTCCCTTCTCTTTATC	ACGTTGGATGCATCATGTTTCTCTGCACAG
rs2410034	ACGTTGGATGTTTAGAGACATTTCTCCTAG	ACGTTGGATGTTAGGATGATGTTAGTTTGG
rs2836437	ACGTTGGATGAGCTTCTGCGATATCAGTGG	ACGTTGGATGTTCCTGTCAGCACATTCTCC
rs2836438	ACGTTGGATGAACATGTCTTGGCCAAGCTC	ACGTTGGATGCCACTGTGACCTCTGGATTT
rs2836439	ACGTTGGATGCCTAGTGTATAAAGTGATGC	ACGTTGGATGTCCTTTCTAGGCACCAATAC
rs2836440	ACGTTGGATGAGATCCTAACCAACCACAGC	ACGTTGGATGAGGTAGGTAGATACAAGGCC
rs2226683	ACGTTGGATGAATATGGCTCCTATAGACAG	ACGTTGGATGTTTTGGGTCACAAAATCAAG

dbSNP rs#	Forward PCR primer	Reverse PCR primer
rs2836441	ACGTTGGATGTTACCTTAATAGTGCTGGCC	ACGTTGGATGACTTTCTGGTCAGAGAGAAG
rs2836442	ACGTTGGATGCAAGGACTCTAGGCTTACAG	ACGTTGGATGGGGACATTTGTAGTCACTTC
rs2836443	ACGTTGGATGGGGCCCCATTACATGTCTAA	ACGTTGGATGTTCGCTGTACTTCCTTCGAG
rs2836444	ACGTTGGATGCTGCAACCAGGAATTGTCAG	ACGTTGGATGAGGACCCATAAAGAGGTGTG
rs3787906	ACGTTGGATGTGAAAAGAGCGGAAATCAAC	ACGTTGGATGGTAAGAAAATCATTCTGTGG
rs3838108	ACGTTGGATGATGAATAAGATGGCAGGCTG	ACGTTGGATGAAGCTGCCCAGATAAAACAG
rs2836445	ACGTTGGATGCATTTCCAAAATTAGACGCAG	ACGTTGGATGAAAAAGAGAAAAACAGATGC
rs2836446	ACGTTGGATGGTGCCTTGTCCTATCAAGAG	ACGTTGGATGAGCATCCAAGCCTGGTAATC
rs3787908	ACGTTGGATGAATCACCACACTAGACCAGC	ACGTTGGATGCATGCAAGGGAAATGTGTGC
rs2836447	ACGTTGGATGATCTCCTCTCTTTGCTCTGC	ACGTTGGATGGAGGAAGGTTAGGAGCTAAG
rs2836448	ACGTTGGATGTGTAGGGATGTATAGGGCAG	ACGTTGGATGAAAGAGAGGAGATCCGTCTG
rs2836450	ACGTTGGATGTGTGGGCATCAGATGACAAC	ACGTTGGATGATCCCGTTAAATGCACCGAC
rs2836451	ACGTTGGATGCAGACAAACAACTGTCACCC	ACGTTGGATGGTATTTCCTTTTCTCGCCGC
rs1015022	ACGTTGGATGTCGAGCCAGCGTCTTTTATC	ACGTTGGATGGTAACAGTCGTACATTCCGG
rs2836452	ACGTTGGATGATCACTGACACAGTCATGAG	ACGTTGGATGCCAGTAACTTTGCAGGTTTG
rs2836453	ACGTTGGATGTGTATTTCCCAAGATGGCCC	ACGTTGGATGCCTCACTTTCTGATGGAAGC
rs3787909	ACGTTGGATGACTTCTCAGTGTTCTGGCTG	ACGTTGGATGCGTCACTCTCTGTTTCATGG
rs2836454	ACGTTGGATGAGGAATGATTCACAACCTCC	ACGTTGGATGGAATGTTCAAATGTAGGGTGG
rs2836455	ACGTTGGATGGGTCTATTGCTGTGACATTT	ACGTTGGATGCATCCCAATTTTTAAGCAAG
rs2155718	ACGTTGGATGAGAACTCTCACACACAGCTG	ACGTTGGATGTGCCTCTTATTACAGCCCTG
rs2836456	ACGTTGGATGGGGATTGTCTGATCTCCTTG	ACGTTGGATGCCAGCTTTCCTTTGTGCATG
rs2836457	ACGTTGGATGAACTCCTGGAATGAGTCACC	ACGTTGGATGATGCACAAAGGAAAGCTGGG
rs2836458	ACGTTGGATGATCACTTAGAAGCCCAGCAG	ACGTTGGATGTGATGCACACTCACTGAAGC
rs2032323	ACGTTGGATGGTAGCCGCACTTTGAGATGC	ACGTTGGATGAGCACAGAGTCGAGGAGGAG
rs2051400	ACGTTGGATGACAGACCTCAGACCAAAGTC	ACGTTGGATGTTTGTCCTAGAGTAACCCCC
rs2836459	ACGTTGGATGGCAAGAATGTTACTTTCTGG	ACGTTGGATGCCATCAAATAGTTGGTTGTC
rs2836460	ACGTTGGATGCAATATCTGAGTTTCACCCC	ACGTTGGATGGTAGATGAGAATTCCGTGTG
rs2836461	ACGTTGGATGGTTACCCACACGGAATTCTC	ACGTTGGATGCCAGATCCAGGTTCTTTCTG
rs2836462	ACGTTGGATGTCTCCTCCGTATGTCTCCAT	ACGTTGGATGATCCCGGAACTCTCTGTTTC
rs2836463	ACGTTGGATGGCACTATTTGACTTGAGCTC	ACGTTGGATGAATTCAAGCCAGAAAGGCTC
rs2836464	ACGTTGGATGGTCTTTTCACCCCAGTAAAG	ACGTTGGATGATAAGCAAAAGGACCTTTGG
rs2836465	ACGTTGGATGTGAGCTCTTGTGTTTTGCCC	ACGTTGGATGGAGAATTCTCCAGCCTTCTC
rs2836466	ACGTTGGATGTGAGCTCTTGTGTTTTGCCC	ACGTTGGATGGAGAATTCTCCAGCCTTCTC
rs2836467	ACGTTGGATGGACTCTGCTCATTTCCTTGG	ACGTTGGATGAAGAGTAGGGGTAGATGCAG
rs3827204	ACGTTGGATGTGAAGATCACACGTGGTGTA	ACGTTGGATGGGGTGAATGCCAAAAAGAGG
rs2836468	ACGTTGGATGTAGAGGCAGGAAAGAGCATG	ACGTTGGATGTTTTTGGCATTCACCCTCTC
rs3787911	ACGTTGGATGTAACCCTCTTCTGGATTCGG	ACGTTGGATGTCATGTGCTCTGAGAGCATC
rs2836469	ACGTTGGATGATTTCTCTACCTCATCCCCC	ACGTTGGATGGGTTGAAGTCACGTAACAGC
rs2836470	ACGTTGGATGCCACTGTTAATCGTATTGCC	ACGTTGGATGACGGACTGAAAGCCAAATGG
rs2212599	ACGTTGGATGAGGAGTTATTCTTCCCCAAC	ACGTTGGATGCAGTGGTCCATTAAGAATCC
rs2836472	ACGTTGGATGGAGTATCGTTCTCTATCATG	ACGTTGGATGTAAAAGAGTCAGAGCAGGAC
rs2836473	ACGTTGGATGTCTCAGCCAGAGTTTTGACC	ACGTTGGATGAATCAACGCCTCCTCTTCAG
rs1888469	ACGTTGGATGACCACCAGGAAGGGTCTGAA	ACGTTGGATGGAGGATCAGAGGCAGAAAAC
rs1888470	ACGTTGGATGGCGTTGATTGCAGTTTTCTG	ACGTTGGATGTTCTTTGGCCTCCGTGTAAG
rs2032322	ACGTTGGATGTGATACTCTGTTGAGCCTCC	ACGTTGGATGGGGGAGCAGTGAGTTATGAGTTAT
rs2410035	ACGTTGGATGAATCACTTGAACCCAGGAGG	ACGTTGGATGTTTTTGAGACGGAGTTTCGC
rs1573332	ACGTTGGATGGGGTGAACTTTACAGAGAGG	ACGTTGGATGCTGCCAGACAGTTTTGAGAC

dbSNP rs#	Forward PCR primer	Reverse PCR primer
rs2836474	ACGTTGGATGAATTCTGCACAGGAGAGTCC	ACGTTGGATGCAGGAAATGAAGATGTCGCC
rs2836475	ACGTTGGATGAGTTCTACATGGGAAGCTGC	ACGTTGGATGATATCTGTGTCTACAGGCCC
rs3787914	ACGTTGGATGGGCTGAAGGCTAAAATCACC	ACGTTGGATGGTCTGAGAAGTAGGAATGGC
rs1888471	ACGTTGGATGACTGAGGCAATTGTGTAGAC	ACGTTGGATGTTGACTTTGTTTTGAGAGGC
rs1888472	ACGTTGGATGTTGCCTCTCAAAACAAAGTC	ACGTTGGATGCTATTATTCTGGAAGCAGCC
rs1888473	ACGTTGGATGAGAAAGTTCAGTTCTCAGCC	ACGTTGGATGTGTTTGCTCCTGTGAGTAAC
rs1888474	ACGTTGGATGTGTTATGTGAGTCCAGGGTG	ACGTTGGATGTCTTGTTATGTGGGTGGGTG
rs2836476	ACGTTGGATGTTACCTGTGACCTCATTTGG	ACGTTGGATGGAACACACAACATACGGTAC
rs3787916	ACGTTGGATGAAGGCATCTCAGTCATTCTC	ACGTTGGATGTGAGTTTGACACAAAGAAGC
rs2836477	ACGTTGGATGTTTAGCTCTCCTGGATGATG	ACGTTGGATGCCATGATTAGTGCATGAAGG
rs970043	ACGTTGGATGTATAACTCCCCTCTCTCCTG	ACGTTGGATGAGAGCAGACCCTTATCAGAG
rs2212600	ACGTTGGATGGAAACAGGTGTTCATTTGGC	ACGTTGGATGTCTGCATGAACCAGTAAGTC
rs2836478	ACGTTGGATGAGCTATTGAGTGTCACTTGC	ACGTTGGATGCAGAAGCTTCTGACTTCAAC
rs2836479	ACGTTGGATGAGTAGCCATCCTAATAGGTG	ACGTTGGATGAGCAAGTGACACTCAATAGC
rs1475877	ACGTTGGATGAATCAACACTCCCCGTGTTC	ACGTTGGATGGGTACCTAGAGTAGTCCAAG
rs2836480	ACGTTGGATGTACCAAACCCACTGTACATC	ACGTTGGATGCATAACCTAACACATTGTGGG
rs2836481	ACGTTGGATGTAAGAAGTTCTTTCTCCCCC	ACGTTGGATGGCTGCTTCTTTCATAAGAGG
rs2836483	ACGTTGGATGCACTGAGGTAATCTCCAACC	ACGTTGGATGGGTGGAGATATGGCTTGATG
rs2836484	ACGTTGGATGAAGCCCACCAGAGTCATCAA	ACGTTGGATGACTACTGACCAGCTTTCCAG
rs2836485	ACGTTGGATGTTCTAAGTGAAGCCCTCCTC	ACGTTGGATGTACAGCTGTGCAAACAGTTG
rs2836486	ACGTTGGATGCATGGTCTGTTGCCTCTAAG	ACGTTGGATGCCCTAGCATTTTATGCATCC
rs2836487	ACGTTGGATGTGAATACCCACTAGGTCTCG	ACGTTGGATGCCACCACTAAACTTAGAGGC
rs1893199	ACGTTGGATGGGCAACAGACCATGGTTTTG	ACGTTGGATGCTTCCCTTCAACATGCACTG
rs2836488	ACGTTGGATGGGCAACAGACCATGGTTTTG	ACGTTGGATGCTTCCCTTCAACATGCACTG
rs1893200	ACGTTGGATGAGTTAAGTCTTCGCATAACC	ACGTTGGATGCCTCTCACACACTAAATCTTG
rs1893201	ACGTTGGATGGTCTTCGCATAACCAAAACAG	ACGTTGGATGCCTCTCACACACTAAATCTTG
rs2836489	ACGTTGGATGGTCAACCATGGAGCTTGAAC	ACGTTGGATGAGAAGACATGTGGGCTTGTG
rs1888475	ACGTTGGATGACCCCTGGCAAGTGAATTAC	ACGTTGGATGGGGAGGTGGATGTTCTTATC
rs2836490	ACGTTGGATGAAAGGCAGAGCTAAAGCAAG	ACGTTGGATGAGCACAACCCAGCAATGCAG
rs2836491	ACGTTGGATGACAACTTGGAGTGGAAAGGG	ACGTTGGATGATCCAGATGGATTCCACAGC
rs2836492	ACGTTGGATGACATATGGGCATGGAAGAGC	ACGTTGGATGAATCCATCTGGATGGAAGAC
rs2836493	ACGTTGGATGTTAAGAGTTCCGATGCTTGC	ACGTTGGATGGTAATCTGGACTTCTCTTCC
rs2836494	ACGTTGGATGGTGCATTCATTTGAATTGCTG	ACGTTGGATGCAGTCTTACTTAAAACTGAC
rs2836495	ACGTTGGATGGAATTTAACGAAACTTCAGC	ACGTTGGATGGGATATTTTCAGGATATCTG
rs2898354	ACGTTGGATGTGTAACAAACCTGCACATCC	ACGTTGGATGGGTACTTTCCAAATATCTGC
rs3065390	ACGTTGGATGCGAGACTCCATCTCAAAAAAG	ACGTTGGATGTGGAAAGTACCAATAGCTTC
rs2836496	ACGTTGGATGTGGAGCTTAATGTGTTCCTG	ACGTTGGATGGTTAGCCATGCATAAGACAG
rs2836497	ACGTTGGATGAGCCGGGATGACTGCTAGAC	ACGTTGGATGAGATGAGGCTGAAGAAGTAA
rs2836498	ACGTTGGATGGGTCCTGGGAAAATAGGATG	ACGTTGGATGCACCCTTGCTCTTTCTGAAG
rs2836499	ACGTTGGATGACTAGTCAGAGCACAGTGAG	ACGTTGGATGGCTCTCTCCTTCTTTGACTC
rs2836500	ACGTTGGATGGCTTCCTGGTTAGTAAGAGG	ACGTTGGATGATCAACTCAGGGCTCTTCTC
rs2836501	ACGTTGGATGACTCACAAAGGTTGACCTTG	ACGTTGGATGGAGGTCCAGGTTGAAAGAAC
rs2836502	ACGTTGGATGGAGGTCCAGGTTGAAAGAAC	ACGTTGGATGACTCACAAAGGTTGACCTTG
rs2836503	ACGTTGGATGGAGCAATTATCAACCCTACG	ACGTTGGATGATTCTCCCCCTTCACTCTTG
rs2836504	ACGTTGGATGGAGTCTGGGTATGGAAAGAG	ACGTTGGATGTTCCTAGAAATGGTGTCTGC
rs3787917	ACGTTGGATGTTTGGAGGAGGAATGCCTTG	ACGTTGGATGCGCCCACAAACCTAAGAGAA
rs2836505	ACGTTGGATGTTTTCGACTGCTCCACTCTG	ACGTTGGATGGCTCTCCCTCATTGTTCTTC

dbSNP rs#	Forward PCR primer	Reverse PCR primer
rs2836506	ACGTTGGATGGGCTAAGGGCATCATTTTATC	ACGTTGGATGGTTTGCTGATTCATGGATGC
rs2836507	ACGTTGGATGAGCAAAGGTTCTGGTGTTGG	ACGTTGGATGAAATGATGCCCTTAGCCCAG
rs2836508	ACGTTGGATGGTGTGATGATATTTTTCTCC	ACGTTGGATGTTTCAGGTATTCCTCTTTGC
rs2836509	ACGTTGGATGTAAAGCTTTCTAAGTCAATG	ACGTTGGATGTCATATGATAATGGTCTCTG
rs2836510	ACGTTGGATGCAGGGAGAGATCTAAACAGC	ACGTTGGATGGCCAAAGCTATAACACGTGG
rs2836511	ACGTTGGATGAGAACCTGACTTTTGGAGTG	ACGTTGGATGCTTCCTCATTGGTCAGAGTC
rs2212601	ACGTTGGATGCCAGCCTTTAGAACTGTGAG	ACGTTGGATGTGGGCTGCTGTAACAAAGTG
rs2212602	ACGTTGGATGACTACAACCAGCCAGAGATG	ACGTTGGATGCACAAACCTTGTGTGAACCC
rs2226682	ACGTTGGATGCCAAGATTGAACCAGGAAAG	ACGTTGGATGCACAAAAGAATTCAGGAGGTG
rs2836512	ACGTTGGATGCCCCAAAACTTAGCATCCTG	ACGTTGGATGTGTTCTCCCTGCACTTCAAC
rs2836513	ACGTTGGATGCACTGGGGTTAGCAAGAAAC	ACGTTGGATGGACTGTGATTCACCCTGTCT
rs1999328	ACGTTGGATGAGTTACAGCGCAAATTGAGG	ACGTTGGATGGCCTTTATGACTCCATTTCTC
rs2212603	ACGTTGGATGTGGAGGGTGTCTGTGAGTAC	ACGTTGGATGTCATGGAGCAAGGTCTGTGG
rs3787919	ACGTTGGATGCCATCAGCTAGGATTCATGG	ACGTTGGATGTCTGTGAGTACCCCACAATG
rs2836514	ACGTTGGATGCAGGTCTAACTAACTGATGAC	ACGTTGGATGGCCTCTACTGTTATTTAAGG
rs1023153	ACGTTGGATGTACAAAAGTGACCTAGAGCC	ACGTTGGATGTTCTTGCAGGAGCATTGTGCC
rs1023372	ACGTTGGATGCAAATTCCAAAATTCTGGTTG	ACGTTGGATGCTCAGAAGTAACATGTACTC
rs2212604	ACGTTGGATGCAGACTTGAGCATATACCAC	ACGTTGGATGACCCATGTGGGAAAATGTTG
rs2226684	ACGTTGGATGGGTGTTGGAAAAGGAACATC	ACGTTGGATGTTAATGATAGTTCCCCTCAG
rs2212605	ACGTTGGATGATATGAGTGATTTGCATGGG	ACGTTGGATGTGCATATAAGCTGTCTGCAC
rs2187307	ACGTTGGATGCACATCCTGCAGCTTTAACC	ACGTTGGATGCCTGGCACTTTCAAGTAACG
rs3065412	ACGTTGGATGGGCTGAGATAGAATGTGCTC	ACGTTGGATGTCTCCTGCTTTGTTCTGGAG
rs2898355	ACGTTGGATGGGCTGAGATAGAATGTGCTC	ACGTTGGATGTCTCCTGCTTTGTTCTGGAG
rs2836518	ACGTTGGATGCACTTGTTGCTTCTTCCACC	ACGTTGGATGATGCCAACCTTGCTGATGTC
rs3838110	ACGTTGGATGGAAGTAGTGAAGTGTTCCCC	ACGTTGGATGAGCCTCACTGAATCTTAACG
rs2836519	ACGTTGGATGTGTTTCTCCTTCTCACTGGG	ACGTTGGATGAAAGGCTACAGGAAGTGAGC
rs3827207	ACGTTGGATGTGTAGTCTGCACCTTCACCT	ACGTTGGATGAGCGGCTGCTGAACATAGAT
rs2836520	ACGTTGGATGCCTGCAAAGGTGTTTGCTTC	ACGTTGGATGGCCACCTAATTTTTCCTCTC
rs2836521	ACGTTGGATGAAGAATAAGAAGCAAACACC	ACGTTGGATGGTTTTAGGGGAAAGGCATAAG
rs2836522	ACGTTGGATGTGCATCTTTGGTTGTGACAG	ACGTTGGATGGCACATCTACTCTTAGCATG
rs2836523	ACGTTGGATGTCTCTCTTTCTTTTCCCTAC	ACGTTGGATGACTCTCAGTTATGATTTCTC
rs2836524	ACGTTGGATGGTGTGTTGGTAGAAACGTTC	ACGTTGGATGGTCACCCCTTCAGATAATAAG
rs2836525	ACGTTGGATGCAGAGCCGAAAACATAGTTC	ACGTTGGATGGTGTGTTGGTAGAAACGTTC
rs3833350	ACGTTGGATGGTTGTTCCTTTTGTCTTCTAG	ACGTTGGATGGAATCATGTCCTTCAGTAAGC
rs2836526	ACGTTGGATGATTGTGTCCTGTCCTGCTAG	ACGTTGGATGGACGGCTAGAAGACAAAAGG
rs2836527	ACGTTGGATGGTGTTTTATGTTCTAGCAGG	ACGTTGGATGGATGCCTTTAGGCAAACATG
rs3834676	ACGTTGGATGAAGCTGAAAAGGATGTGCAG	ACGTTGGATGACAGGGCATACTTCTCTATC
rs2836528	ACGTTGGATGCCAAAACTCATGCGATCTGC	ACGTTGGATGTGGCGCTGAAGTACTCAATG
rs3761364	ACGTTGGATGAAACAGCACAGCTACCATTC	ACGTTGGATGATGAGAAAATGTGTGTGGAG
rs2836529	ACGTTGGATGAGCGGTGTTTTAAAATGTCC	ACGTTGGATGCAGAGCCCAAAAAAAATTTGG
rs2836530	ACGTTGGATGACAGACAGTGGTCAGAACAT	ACGTTGGATGAAAGATGCCTATAATCCAGG
rs3761366	ACGTTGGATGCAGGTGATAAAAAGCAAGTG	ACGTTGGATGGCCATCAGTTCTTTTTTGGC
rs2836531	ACGTTGGATGGCCTTCGAAAATGTCTCAAG	ACGTTGGATGCACTTGCTTTTTATCACCTG
rs2836532	ACGTTGGATGGAAAGACAGCCTTCGAAAATG	ACGTTGGATGCAATGGCTCTTTGCAGTAAC
rs2836533	ACGTTGGATGTTTCTGACCTCTCACGGTAC	ACGTTGGATGTGCAGATCTGGAGGTAGATG
rs2836534	ACGTTGGATGAGAAGAGGCTGGGAGAGGAT	ACGTTGGATGTGCTGCTCTTAGGATAAGGG
rs2836535	ACGTTGGATGACAGGAGGAGTTGAGTGTTG	ACGTTGGATGTAGAGGCACGGAGAAGATAG

dbSNP rs#	Forward PCR primer	Reverse PCR primer
rs2836536	ACGTTGGATGAAAAGCATGGGTACAGGAGG	ACGTTGGATGTAGAGGCACGGAGAAGATAG
rs3827208	ACGTTGGATGGAGGATGAGAGGTACCTGAG	ACGTTGGATGGGGATGATCAAACGTAGT
rs715860	ACGTTGGATGTTCTGGTGGAGGTTTCTTGG	ACGTTGGATGCGAGACATGATCTCAAACCC
rs717231	ACGTTGGATGCAAGAGACTCAAACAGTTGC	ACGTTGGATGTCATAGAAGTTACAGCAGCC
rs2836537	ACGTTGGATGTTGGTGTGTGATCACTCTGG	ACGTTGGATGGAACCTAAGTTTCTCCCAGC
rs2836538	ACGTTGGATGGGTTAGAGCTTACGTAATTC	ACGTTGGATGCTACTTGTGTCACTTCTTTG
rs2836539	ACGTTGGATGTTATCCTCCAAGAGCCTTAG	ACGTTGGATGGGGCAAATGGAGTTCTTATT
rs2836540	ACGTTGGATGCCCAGTTGGTATCAGTGTTG	ACGTTGGATGTGCTGAACATCGTTTGGAGG
rs2836541	ACGTTGGATGCTTGCACTGACACCTTTGTG	ACGTTGGATGGTACTGGCGAAGACATGATG
rs2836542	ACGTTGGATGAGATGAGCCATTTCCTACTG	ACGTTGGATGCAGCATGAGAAACTGAATGC
rs2836543	ACGTTGGATGAAATGGACTTCTTCAGTAGG	ACGTTGGATGGATACAATTCAACCCATAGC
rs881837	ACGTTGGATGAATGGATGTGGCTCTTGAGG	ACGTTGGATGTATGGAGGGACTTACGAAAG
rs3949052	ACGTTGGATGTTTTCAACGGAAACAGATGC	ACGTTGGATGCCAAGTAAAATATTCAATCCCC
rs2065307	ACGTTGGATGTTTTCAACGGAAACAGATGC	ACGTTGGATGCCAAGTAAAATATTCAATCCCC
rs3216105	ACGTTGGATGACCACCATGCCTGGCTAATT	ACGTTGGATGGGCCTGGACAAAATAGTGAG
rs2073427	ACGTTGGATGTTTTGCTTGGGTGTTCTGCC	ACGTTGGATGGGATTTACACTGGTGTTGGG

TABLE 30

dbSNP rs#	Extend Primer	Term Mix
Rs2898353	TCCTGTCTTCAGTGCTTGATTCTG	CGT
rs960818	AGTAGATAACATAAAGTAACCAGC	ACT
rs960819	GCTATTCACCCTAGCTGTACATAG	ACT
Rs2410034	AAATGTAGCTGTAGTATCTTGAA	ACT
Rs2836437	TTCACACTCAACAACAAACACA	ACT
Rs2836438	TGGAAAGTAAGCTAGACCAAACAG	ACT
Rs2836439	GTATAAAGTGATGCTGCTTGC	ACT
Rs2836440	AACAATTGGGATATGTCTCTCCAC	ACG
Rs2226683	GAGAGTTAATGTGCCCTACTT	ACT
Rs2836441	TAATAGTGCTGGCCATAATGC	ACT
Rs2836442	CTCTAGGCTTACAGTAAACAC	ACT
Rs2836443	TATAAGTTCAGGGTCACAGGTC	ACT
Rs2836444	TGTGTTCTTGGGGTCGCCT	ACT
Rs3787906	TAATGTAGGTGCTGAGAACTTAG	ACT
Rs3838108	GGCTGATTAAAATTCTGTTTCCCC	ACT
Rs2836445	AGACGCAGTAAAACTTATGGAT	ACG
Rs2836446	GCCTTGTCCTATCAAGAGCCAAAG	CGT
Rs3787908	CATACAGTAGCTGTGGACAGC	ACT
Rs2836447	ATGTATTACATTGAGAACCATGTG	ACT
Rs2836448	TGTATAGGGCAGGGATAAAGAC	ACT
Rs2836450	AACAACAAATTTACTGATATCATC	ACT
Rs2836451	CTGTCACCCATTGACCTCAC	ACT
Rs1015022	CTTTTATCTGCAGTTGCACCC	ACT
Rs2836452	CGGGAAGATGGCTGCCTTC	ACG

dbSNP rs#	Extend Primer	Term Mix
Rs2836453	CCAAGATGGCCCAGTAGGA	CGT
Rs3787909	AAATAGTAAAATAAAAAGAGCTCC	ACG
Rs2836454	CACAACCTCCCAAATGAATAAATC	ACT
Rs2836455	TGCTGTGACATTTTAGTGCTTCTG	CGT
Rs2155718	CTCACACACAGCTGGAGTTTA	ACT
Rs2836456	CGTTCTGAAGGTTTTGTGTACA	ACT
Rs2836457	GAGTCACCCGTCCCCTAGA	ACT
Rs2836458	ACAGAAGAGCCAGCCGACA	ACT
Rs2032323	TGCACACTCACTGAAGCCC	ACT
Rs2051400	AAACACTATGTGACGCCACC	ACT
Rs2836459	AGAATGTTACTTTCTGGATTCTAC	ACT
Rs2836460	ATTGTAATTCTCCGTAAAACCC	ACG
Rs2836461	TACCCACACGGAATTCTCATCTAC	ACT
Rs2836462	TCCGTATGTCTCCATCCATCTCA	ACT
Rs2836463	AAACTTAAATTGCTTTAATCAGCT	ACT
Rs2836464	AATATCTTATCACTGCTCCTGTCT	ACG
Rs2836465	GCCCACTTTTGTGTTTGCTTTAG	ACT
Rs2836466	TTTGCCCACTTTTGTGTTTGCT	ACT
Rs2836467	TTAATTTTCTTGTCTCTTTCTGTA	ACT
Rs3827204	CCCTCACATCTTCCCCGC	ACT
Rs2836468	GCAGGAAAGAGCATGGGCATTAAC	ACT
Rs3787911	TACATCCAAAAGCCTGCCAG	ACT
Rs2836469	TCCTGCGAGATCCTGCTCA	ACG
Rs2836470	ACAAGCTTAATGTTTTGTTCAGA	ACT
Rs2212599	TTCCCCAACAATAGTCAGAAAA	ACT
Rs2836472	TTCTCTATCATGATGCAGTCC	ACT
Rs2836473	GATGATGAACAGGGCTGTGA	ACG
Rs1888469	AAGGGTCTGAAGAGGAGGC	ACT
Rs1888470	GTTTTCTGCCTCTGATCCTCA	ACT
Rs2032322	CCTATAGGTAACGTGGCTTCT	ACT
Rs2410035	AGGCAGAAGTTGCAGTGAAC	ACG
Rs1573332	GAGAGGCCAGAAAGCCTTC	CGT
Rs2836474	GCACAGGAGAGTCCTCAATT	ACG
Rs2836475	CATGGGAAGCTGCTGAACTA	ACT
Rs3787914	ACAGTGTTTGAGCCCTCCTT	ACT
Rs1888471	AACTGACAGAAGAAAGAAAAATAT	ACG
Rs1888472	TGTGTTGGTGTATAAATCAAGATT	ACG
Rs1888473	CAGTTCTCAGCCAGACGATC	ACG
Rs1888474	GAGTCCAGGGTGCTAATTTC	ACG
Rs2836476	GGTGTTAGCCCTGGGTTCTAATAA	ACG
Rs3787916	TCTCTTATGTAAATACAAAGACG	CGT
Rs2836477	CCTCTTAAAATAGCCTGCCTTCA	ACT
rs970043	GCTCCTTGACTCAAGTATTTC	ACG
Rs2212600	AAAACAACTTTCTCTCCCAAAC	ACG

dbSNP rs#	Extend Primer	Term Mix
Rs2836478	CTTGCTTATCTTCAAGCAGTC	CGT
Rs2836479	CCTAATAGGTGTGAAGTGTAAAA	CGT
Rs1475877	CTCCCCGTGTTCTGCATGC	ACG
Rs2836480	CCCACTGTACATCTTACACTC	ACT
Rs2836481	TCCCCCTGAAATCCCATAGC	ACT
Rs2836483	AGGTAATCTCCAACCAAACCT	ACT
Rs2836484	AGTCATCAAGCCATATCTCCA	ACG
Rs2836485	CTCCTCTGGGACGTCAGC	ACT
Rs2836486	CCTCTAAGTTTAGTGGTGGAT	ACT
Rs2836487	TGTTGGGTTCTACACATTCAAA	ACT
Rs1893199	CAGACCATGGTTTTGAATGTG	ACG
Rs2836488	GTAGAACCCAACACAGAGCC	ACG
Rs1893200	AGTCTTCGCATAACCAAAACAGA	ACT
Rs1893201	CGCATAACCAAAACAGAAAAGAAC	ACT
Rs2836489	CAAGAGCTCTTTTCAATTCCAG	ACT
Rs1888475	GACATCAAATGATTCCCCTGT	ACT
Rs2836490	GAGCCAAAGCTTTCCTGATG	ACT
Rs2836491	GTGGAAAGGGCACTGTGGT	ACT
Rs2836492	GGCATGGAAGAGCAAGCATC	ACT
Rs2836493	TCCGATGCTTGCTCTTCCAT	ACT
Rs2836494	TGAAGTTTCGTTAAATTCACTACA	ACT
Rs2836495	CTTCAGCAATTCAAATGAATGCAC	ACT
Rs2898354	TCCGGCACATATATCCTGGAAC	ACT
Rs3065390	AAACAAACAAACAAAAACAGTGTA	ACT
Rs2836496	GTGTTCCTGATGTTTCTGGAGT	CGT
Rs2836497	CTGCTAGACATTGTCAGTCC	ACT
Rs2836498	AATAGGATGAGTCAAAGAAGGAG	ACT
Rs2836499	GAGAAGAGCCCTGAGTTGATAAA	ACT
Rs2836500	AGAGGATGAGCAATTTCAGGGA	ACT
Rs2836501	CAAAGGTTGACCTTGTTTTCTAT	CGT
Rs2836502	AAGAACTTACATTTTATGGCTTC	ACT
Rs2836503	GATTTGGGAGCAAGGGAGC	ACT
Rs2836504	AGAGTTAAAGATGACTCTAGGCTC	ACT
Rs3787917	GCAGCCAGAGTGGAGCAGT	ACG
Rs2836505	AAGGCATTCCTCCTCCAAATCAC	ACT
Rs2836506	GAAAATCAAATCAGTTTCTACAAC	ACT
Rs2836507	GTGTTGGAATATTGTTGGCCT	ACT
Rs2836508	ATTCTCTACCATTTCATTCTCTTT	ACT
Rs2836509	TTTCTAAGTCAATGTAGGCAAC	ACT
Rs2836510	CAGCTAGTTATCTTACTTCACC	ACT
Rs2836511	AGCAGGTGACAACCCAGACAT	ACT
Rs2212601	TAAGTTTCTGTTGTTTATATGCCA	ACT
Rs2212602	CCAGCCAGAGATGGGATCA	ACG
Rs2226682	GATTGAACCAGGAAAGAAATAGTT	CGT

dbSNP rs#	Extend Primer	Term Mix
Rs2836512	AATGCCAGTTGCCATAGGATA	ACG
Rs2836513	ATAAGAAGATGAGTACTATTATTG	ACT
Rs1999328	ATTGAGGGAAGAGTAAATGATTTC	CGT
Rs2212603	TGTCTGTGAGTACCCCACAATGAA	ACT
Rs3787919	TCTGTGGCTTCAATGCTGGG	ACT
Rs2836514	ACAGACTTTAACAAAATCACTGA	ACT
Rs1023153	GGGTCATCTCCTTACCTGTCCAA	ACG
Rs1023372	TTCCAAAATTCTGGTTGTGTTTT	ACT
Rs2212604	CTGCCCCTATACATACATAGCTTC	ACG
Rs2226684	AAAAACAATCTGCACAACAAATAT	ACT
Rs2212605	GCAGTGAATATGAACAAAAAAAAA	ACT
Rs2187307	CAGCTTTAACCTCACTCCAC	ACT
Rs3065412	AGTTACAAATCAGGTGGTGCTGG	ACT
Rs2898355	GTTACAAATCAGGTGGTGCTG	ACT
Rs2836518	TAGGAATCGGAGTCAATAATTTT	ACT
Rs3838110	GCTGCACAATCCCCCCCC	CGT
Rs2836519	CCTTCTCACTGGGTTCCTG	ACG
Rs3827207	TATCACCCCTGTGTCCTGC	ACG
Rs2836520	CACAAATAGATTATATATCCTGTT	ACT
Rs2836521	AATAAGAAGCAAACACCTTTGCA	ACT
Rs2836522	CCACCCCTTCAGAGAGTTG	ACT
Rs2836523	TCATATTGGTTGATCGTATTGGTT	ACT
Rs2836524	GATTTCAGGAATGAACTATGTTTT	ACG
Rs2836525	AGCCGAAAACATAGTTCATTCCTG	ACT
Rs3833350	CTTTTGTCTTCTAGCCGTCAG	ACT
Rs2836526	AGAACATAAAACACAGAAATGCA	ACT
Rs2836527	TTATGTTCTAGCAGGACAGGA	CGT
Rs3834676	AAAAGGATGTGCAGATCGCAT	ACT
Rs2836528	ATCTGCACATCCTTTTCAGCTT	ACG
Rs3761364	CTACCATTCATTGAGTACTTCAG	ACG
Rs2836529	CTTCAAAATGTGGGTTGATACC	ACT
Rs2836530	GGTCAGAACATGCTGCTTTAT	ACT
Rs3761366	GTGATGGCTTCTAAAAATGTAAA	ACG
Rs2836531	GCATTTGTTACTGCAAAGAGCCAT	ACG
Rs2836532	AGCCTTCGAAAATGTCTCAAG	CGT
Rs2836533	CACACCCATTCCAACCCAAT	ACG
Rs2836534	GCTGAAGGTTTCTGGGAGCA	ACG
Rs2836535	GAGGAGTTGAGTGTTGGAACCA	ACG
Rs2836536	ATGGGTACAGGAGGAGTTGA	ACT
Rs3827208	CACCCACCCCAATCACCC	ACT
rs715860	CTTGGTTATCCTTCAGTTTCCA	ACT
rs717231	CTCATTTAGTTTATGTCTTGGTTG	ACT
Rs2836537	GCTCATACGCCCTTGGTCTCTAAT	ACT
Rs2836538	AGCTTACGTAATTCAAATCAAGT	ACT

dbSNP rs#	Extend Primer	Term Mix
Rs2836539	TTACACATTTGCACAATGAGGATA	CGT
Rs2836540	GTATCAGTGTTGAATGACTGGT	ACT
Rs2836541	TGACACCTTTGTGAATTGCTGAAC	ACT
Rs2836542	CCATTTCCTACTGAAGAAGTCCA	ACT
Rs2836543	CTTCTTCAGTAGGAAATGGCT	ACG
rs881837	GGCTCTTGAGGCCATGCC	ACG
Rs3949052	ACAATTTCTCATGTTGTAAGGATT	ACG
Rs2065307	GGAAACAGATGCCATTTACAATTT	ACG
Rs3216105	GCCTGGCTAATTTTTTAAAAAAAAA	CGT
Rs2073427	CTGCCCCCACATGACCCA	ACG

Genetic Analysis

[0254] Allelotyping results from the discovery cohort are shown for cases and controls in Table 31. The allele frequency for the A2 allele is noted in the fifth and sixth columns for osteoarthritis case pools and control pools, respectively, where "AF" is allele frequency. The allele frequency for the A1 allele can be easily calculated by subtracting the A2 allele frequency from 1 (A1 AF = 1-A2 AF). For example, the SNP rs2898353 has the following case and control allele frequencies: case A1 (A) = 0.79; case A2 (T) = 0.21; control A1 (A) = 0.81; and control A2 (T) = 0.19, where the nucleotide is provided in paranthesis. Some SNPs are labeled "untyped" because of failed assays.

TABLE 31

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2898353	231	38783681	A/T	0.21	0.19	0.560
rs960818	882	38784332	A/G	0.59	0.57	0.330
rs960819	960	38784410	A/C	0.13	0.09	0.101
rs2410034	1194	38784644	A/C			
rs2836437	1530	38784980	A/G	0.14	0.14	0.956
rs2836438	1673	38785123	A/G	0.79	0.75	0.077
rs2836439	2096	38785546	C/T	0.70	0.71	0.508
rs2836440	2285	38785735	A/G	0.19	0.18	0.623
rs2226683	5873	38789323	C/T	0.79	0.76	0.312
rs2836441	7256	38790706	A/G	0.12	0.12	0.765
rs2836442	7988	38791438	A/G	0.31	0.30	0.746
rs2836443	8222	38791672	G/T	0.22	0.23	0.728
rs2836444	8381	38791831	C/T	0.19	0.20	0.807
rs3787906	8814	38792264	C/T	0.97	untyped	NA
rs3838108	8915	38792365	-/C	0.58	0.56	0.425
rs2836445	9642	38793092	A/G	0.32	0.35	0.190
rs2836446	9902	38793352	A/T	0.12	0.14	0.274
rs3787908	10619	38794069	A/G			
rs2836447	10927	38794377	C/T	0.68	0.67	0.816
rs2836448	11032	38794482	C/T	0.12	0.14	0.235
rs2836450	14377	38797827	C/T	0.70	0.68	0.460
rs2836451	15608	38799058	C/T	0.92	0.95	0.157

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs1015022	15928	38799378	C/G	0.31	0.36	0.072
rs2836452	16296	38799746	A/G	0.18	0.18	0.822
rs2836453	17598	38801048	A/T	0.02	0.02	0.836
rs3787909	19272	38802722	A/G	0.06	0.03	0.091
rs2836454	20084	38803534	A/G	0.04	0.03	0.397
rs2836455	20577	38804027	A/T	0.17	0.13	**0.050**
rs2155718	28051	38811501	A/G	0.78	0.78	0.950
rs2836456	29466	38812916	A/G	0.94	0.92	0.569
rs2836457	29530	38812980	C/T			
rs2836458	29987	38813437	A/G	0.48	0.46	0.455
rs2032323	30012	38813462	C/T			
rs2051400	30322	38813772	G/T	0.03	NA	NA
rs2836459	32216	38815666	C/T	0.19	0.17	0.319
rs2836460	32516	38815966	C/T			
rs2836461	32544	38815994	A/G			
rs2836462	32746	38816196	A/G			
rs2836463	33137	38816587	G/T	0.67	0.72	**0.032**
rs2836464	33538	38816988	A/G	0.67	0.67	0.991
rs2836465	33798	38817248	C/T			
rs2836466	33802	38817252	A/C	0.39	0.40	0.627
rs2836467	33964	38817414	C/T			
rs3827204	34132	38817582	A/G	0.45	0.42	0.213
rs2836468	34210	38817660	C/T	0.13	0.14	0.678
rs3787911	34317	38817767	A/G	0.13	0.12	0.862
rs2836469	34499	38817949	C/T	0.38	0.40	0.250
rs2836470	34753	38818203	A/C	0.73	0.74	0.939
rs2212599	34845	38818295	C/T	0.66	0.64	0.474
rs2836472	35335	38818785	C/T	0.40	0.35	0.071
rs2836473	36423	38819873	C/T	0.53	0.54	0.755
rs1888469	36450	38819900	A/G	0.45	0.49	0.175
rs1888470	36481	38819931	G/T	0.17	0.18	0.623
rs2032322	38447	38821897	C/G	0.50	0.50	0.879
rs2410035	38784	38822234	C/T			
rs1573332	39387	38822837	A/T	0.57	0.58	0.609
rs2836474	39458	38822908	C/T	0.33	0.35	0.564
rs2836475	39822	38823272	C/G	0.17	0.14	0.113
rs3787914	40305	38823755	C/G	0.73	0.73	0.987
rs1888471	40869	38824319	C/T	0.29	0.26	0.175
rs1888472	40926	38824376	C/T	0.62	0.63	0.818
rs1888473	41010	38824460	C/T	0.63	0.65	0.435
rs1888474	41134	38824584	C/T	0.28	0.23	0.099
rs2836476	41984	38825434	A/G	0.46	0.44	0.379
rs3787916	42172	38825622	A/T	0.45	0.43	0.314
rs2836477	42753	38826203	G/T	0.94	0.96	0.196
rs970043	43011	38826461	C/T	0.04	0.04	0.549
rs2212600	43176	38826626	A/G			
rs2836478	43320	38826770	G/T	0.76	0.75	0.914
rs2836479	43381	38826831	A/T	0.44	0.43	0.670
rs1475877	44142	38827592	A/G	0.35	0.32	0.110
rs2836480	44383	38827833	A/G	0.46	0.43	0.153
rs2836481	44726	38828176	C/T	0.42	0.40	0.434
rs2836483	45087	38828537	A/G	0.47	0.45	0.393
rs2836484	45141	38828591	C/T	0.46	0.47	0.671
rs2836485	45359	38828809	C/G	0.16	0.17	0.643
rs2836486	45421	38828871	C/T			
rs2836487	45456	38828906	C/T	0.02	0.03	0.758
rs1893199	45467	38828917	C/T	0.62	0.65	0.220

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2836488	45486	38828936	C/T	0.25	0.23	0.360
rs1893200	45709	38829159	A/G	0.16	0.14	0.177
rs1893201	45716	38829166	A/G	0.84	0.87	0.060
rs2836489	47626	38831076	C/T	0.29	0.31	0.502
rs1888475	49413	38832863	A/G			
rs2836490	49796	38833246	C/T	0.94	0.93	0.731
rs2836491	49962	38833412	A/G	0.10	0.08	0.219
rs2836492	50075	38833525	C/T	0.20	0.22	0.518
rs2836493	50093	38833543	A/G	0.95	0.94	0.850
rs2836494	50571	38834021	C/T	0.72	0.70	0.536
rs2836495	50615	38834065	A/G	0.82	0.78	0.142
rs2898354	50780	38834230	A/G	0.25	0.25	0.728
rs3065390	50851	38834301	-/TA	0.10	0.11	0.845
rs2836496	51459	38834909	A/C	0.80	0.84	0.064
rs2836497	53193	38836643	C/T	0.65	0.65	0.935
rs2836498	53702	38837152	C/T	0.43	0.44	0.682
rs2836499	53736	38837186	A/C	0.33	0.30	0.169
rs2836500	53795	38837245	C/T			
rs2836501	54109	38837559	A/T	0.36	0.34	0.234
rs2836502	54126	38837576	C/T	0.31	0.29	0.427
rs2836503	54230	38837680	A/C	0.32	0.29	0.194
rs2836504	54894	38838344	C/T	0.51	0.54	0.170
rs3787917	55455	38838905	A/G	0.56	0.60	0.137
rs2836505	55499	38838949	A/G	0.73	0.78	0.022
rs2836506	56522	38839972	C/T	0.52	0.56	0.145
rs2836507	56662	38840112	C/T	0.51	0.54	0.173
rs2836508	56954	38840404	A/G	0.53	0.56	0.376
rs2836509	57267	38840717	A/G	0.35	0.31	0.089
rs2836510	58282	38841732	A/G	0.65	0.59	0.034
rs2836511	58916	38842366	A/C	0.32	0.30	0.315
rs2212601	59544	38842994	C/G	0.45	0.46	0.568
rs2212602	59666	38843116	C/T	0.30	0.28	0.644
rs2226682	59913	38843363	A/T	0.38	0.35	0.164
rs2836512	66846	38850296	A/G	0.94	0.94	0.896
rs2836513	67245	38850695	G/T	0.23	0.22	0.713
rs1999328	67652	38851102	A/C	0.79	0.79	0.973
rs2212603	67955	38851405	A/G	0.73	0.72	0.776
rs3787919	67966	38851416	A/C			
rs2836514	68420	38851870	A/G	0.52	0.54	0.319
rs1023153	70226	38853676	A/G	0.09	0.09	0.985
rs1023372	70810	38854260	C/T	0.83	0.81	0.518
rs2212604	72246	38855696	A/G	0.68	0.71	0.237
rs2226684	73330	38856780	G/T	0.83	0.81	0.462
rs2212605	73457	38856907	C/T	0.82	0.85	0.255
rs2187307	74389	38857839	A/G	0.13	0.13	0.869
rs3065412	74638	38858088	-/AA			
rs2898355	74640	38858090	A/C	0.96	0.94	0.413
rs2836518	75358	38858808	A/C	0.10	0.12	0.261
rs3838110	75952	38859402	-/G	0.66	0.67	0.790
rs2836519	76098	38859548	A/G	0.60	0.61	0.509
rs3827207	77836	38861286	A/G	0.62	0.63	0.575
rs2836520	78449	38861899	A/C			
rs2836521	78507	38861957	G/T	0.07	0.08	0.551
rs2836522	80031	38863481	G/T	0.11	0.08	0.155
rs2836523	81695	38865145	C/T			
rs2836524	82775	38866225	A/G	0.05	0.04	0.321
rs2836525	82795	38866245	A/G	0.11	0.11	0.875

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs3833350	84611	38868061	-/C			
rs2836526	84657	38868107	C/T	0.83	0.86	0.292
rs2836527	84693	38868143	A/C	0.08	0.08	0.936
rs3834676	85020	38868470	-/T	0.80	0.83	0.191
rs2836528	85048	38868498	C/T	0.84	0.87	0.089
rs3761364	85100	38868550	C/T	0.06	0.04	0.159
rs2836529	85325	38868775	A/C	0.09	0.06	0.100
rs2836530	85452	38868902	C/T			
rs3761366	85868	38869318	A/G	0.06	0.04	0.179
rs2836531	85936	38869386	A/G	0.49	0.50	0.729
rs2836532	85990	38869440	A/T	0.30	0.29	0.766
rs2836533	86139	38869589	C/T	0.47	0.48	0.751
rs2836534	86497	38869947	C/T	0.87	0.87	0.874
rs2836535	87236	38870686	A/G	0.93	0.92	0.628
rs2836536	87248	38870698	C/T	0.86	0.84	0.474
rs3827208	87533	38870983	C/G	0.51	0.53	0.459
rs715860	87912	38871362	A/G	0.08	0.09	0.627
rs717231	88108	38871558	G/T	0.65	0.67	0.382
rs2836537	88494	38871944	A/C	0.43	0.40	0.239
rs2836538	89598	38873048	A/C			
rs2836539	90235	38873685	A/T	0.98	0.97	0.796
rs2836540	91287	38874737	G/T			
rs2836541	91359	38874809	C/T	0.07	0.06	0.403
rs2836542	92384	38875834	A/C	0.36	0.38	0.418
rs2836543	92410	38875860	C/T	0.54	0.50	0.202
rs881837	92900	38876350	C/T	0.29	0.28	0.639
rs3949052	94495	38877945	A/G			
rs2065307	94512	38877962	A/G			
rs3216105	97777	38881227	-/A	0.32	0.28	0.265
rs2073427	98333	38881783	C/T	0.09	0.07	0.242

[0255] The *ERG* proximal SNPs were also allelotyped in the replication cohorts using the methods described herein and the primers provided in Tables 29 and 30. The replication allelotyping results for replication cohort #1 and replication cohort #2 are provided in Tables 32 and 33, respectively.

TABLE 32

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2898353	231	38783681	A/T	0.19	0.19	0.773
rs960818	882	38784332	A/G	0.59	0.57	0.600
rs960819	960	38784410	A/C	0.07	NA	0.132
rs2410034	1194	38784644	A/C			
rs2836437	1530	38784980	A/G	0.14	0.14	0.957
rs2836438	1673	38785123	A/G	0.80	0.77	0.402
rs2836439	2096	38785546	C/T	0.68	0.73	0.089
rs2836440	2285	38785735	A/G	0.20	0.18	0.421
rs2226683	5873	38789323	C/T	0.78	0.76	0.622
rs2836441	7256	38790706	A/G	0.12	0.12	0.946
rs2836442	7988	38791438	A/G	0.30	0.32	0.674
rs2836443	8222	38791672	G/T	0.22	0.25	0.332
rs2836444	8381	38791831	C/T	0.20	0.20	0.908
rs3787906	8814	38792264	C/T	0.97	untyped	NA

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs3838108	8915	38792365	-/C	0.58	0.56	0.604
rs2836445	9642	38793092	A/G	0.33	0.37	0.211
rs2836446	9902	38793352	A/T	0.13	0.15	0.481
rs3787908	10619	38794069	A/G			
rs2836447	10927	38794377	C/T	0.67	0.67	0.843
rs2836448	11032	38794482	C/T	0.13	0.15	0.521
rs2836450	14377	38797827	C/T	0.67	0.67	0.989
rs2836451	15608	38799058	C/T	0.92	0.95	0.214
rs1015022	15928	38799378	C/G	0.30	0.36	0.076
rs2836452	16296	38799746	A/G	0.18	0.18	0.982
rs2836453	17598	38801048	A/T	0.02	untyped	NA
rs3787909	19272	38802722	A/G	0.06	0.03	0.110
rs2836454	20084	38803534	A/G	0.03	0.03	0.746
rs2836455	20577	38804027	A/T	0.17	0.12	0.080
rs2155718	28051	38811501	A/G	0.78	0.79	0.747
rs2836456	29466	38812916	A/G	0.91	0.91	0.915
rs2836457	29530	38812980	C/T			
rs2836458	29987	38813437	A/G	0.48	0.47	0.626
rs2032323	30012	38813462	C/T			
rs2051400	30322	38813772	G/T	0.02	untyped	NA
rs2836459	32216	38815666	C/T	0.20	0.16	0.278
rs2836460	32516	38815966	C/T			
rs2836461	32544	38815994	A/G			
rs2836462	32746	38816196	A/G			
rs2836463	33137	38816587	G/T	0.67	0.75	**0.011**
rs2836464	33538	38816988	A/G	0.66	0.68	0.586
rs2836465	33798	38817248	C/T			
rs2836466	33802	38817252	A/C	0.39	0.41	0.507
rs2836467	33964	38817414	C/T			
rs3827204	34132	38817582	A/G	0.45	0.41	0.229
rs2836468	34210	38817660	C/T	0.13	0.14	0.736
rs3787911	34317	38817767	A/G	0.14	0.13	0.856
rs2836469	34499	38817949	C/T	0.37	0.41	0.168
rs2836470	34753	38818203	A/C	0.72	0.73	0.854
rs2212599	34845	38818295	C/T	0.63	0.65	0.636
rs2836472	35335	38818785	C/T	0.41	0.35	0.145
rs2836473	36423	38819873	C/T	0.51	0.54	0.291
rs1888469	36450	38819900	A/G	0.45	0.49	0.281
rs1888470	36481	38819931	G/T	0.17	0.17	0.949
rs2032322	38447	38821897	C/G	0.51	0.53	0.476
rs2410035	38784	38822234	C/T			
rs1573332	39387	38822837	A/T	0.56	0.60	0.279
rs2836474	39458	38822908	C/T	0.33	0.36	0.330
rs2836475	39822	38823272	C/G	0.18	0.13	**0.049**
rs3787914	40305	38823755	C/G	0.73	0.74	0.977
rs1888471	40869	38824319	C/T	0.31	0.26	0.134
rs1888472	40926	38824376	C/T	0.62	0.65	0.247
rs1888473	41010	38824460	C/T	0.63	0.67	0.210
rs1888474	41134	38824584	C/T	0.28	0.21	0.091
rs2836476	41984	38825434	A/G	0.47	0.44	0.346
rs3787916	42172	38825622	A/T	0.46	0.41	0.171
rs2836477	42753	38826203	G/T	0.94	0.97	0.294
rs970043	43011	38826461	C/T	0.05	0.03	0.331
rs2212600	43176	38826626	A/G			
rs2836478	43320	38826770	G/T	0.75	0.75	0.983
rs2836479	43381	38826831	A/T	0.44	0.43	0.752
rs1475877	44142	38827592	A/G	0.35	0.31	0.166

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2836480	44383	38827833	A/G	0.45	0.41	0.254
rs2836481	44726	38828176	C/T	0.42	0.39	0.330
rs2836483	45087	38828537	A/G	0.46	0.46	0.797
rs2836484	45141	38828591	C/T	0.45	0.47	0.553
rs2836485	45359	38828809	C/G	0.18	0.18	0.993
rs2836486	45421	38828871	C/T			
rs2836487	45456	38828906	C/T	0.03	0.03	0.955
rs1893199	45467	38828917	C/T	0.61	0.67	0.071
rs2836488	45486	38828936	C/T	0.27	0.23	0.246
rs1893200	45709	38829159	A/G	0.16	0.13	0.203
rs1893201	45716	38829166	A/G	0.83	0.89	**0.021**
rs2836489	47626	38831076	C/T	0.30	0.31	0.702
rs1888475	49413	38832863	A/G			
rs2836490	49796	38833246	C/T	0.94	0.95	0.662
rs2836491	49962	38833412	A/G	0.10	0.06	**0.038**
rs2836492	50075	38833525	C/T	0.20	0.22	0.651
rs2836493	50093	38833543	A/G	0.93	0.95	0.397
rs2836494	50571	38834021	C/T	0.73	0.71	0.592
rs2836495	50615	38834065	A/G	0.81	0.77	0.212
rs2898354	50780	38834230	A/G	0.24	0.24	0.827
rs3065390	50851	38834301	-/TA	0.10	0.11	0.743
rs2836496	51459	38834909	A/C	0.78	0.86	**0.022**
rs2836497	53193	38836643	C/T	0.65	0.66	0.733
rs2836498	53702	38837152	C/T	0.44	0.46	0.576
rs2836499	53736	38837186	A/C	0.33	0.29	0.200
rs2836500	53795	38837245	C/T			
rs2836501	54109	38837559	A/T	0.36	0.32	0.167
rs2836502	54126	38837576	C/T	0.31	0.27	0.206
rs2836503	54230	38837680	A/C	0.32	0.28	0.173
rs2836504	54894	38838344	C/T	0.50	0.57	**0.033**
rs3787917	55455	38838905	A/G	0.56	0.62	**0.033**
rs2836505	55499	38838949	A/G	0.72	0.81	**0.004**
rs2836506	56522	38839972	C/T	0.52	0.58	0.093
rs2836507	56662	38840112	C/T	0.51	0.56	0.134
rs2836508	56954	38840404	A/G	0.53	0.58	0.170
rs2836509	57267	38840717	A/G	0.35	0.30	0.136
rs2836510	58282	38841732	A/G	0.62	0.56	**0.035**
rs2836511	58916	38842366	A/C	0.33	0.30	0.273
rs2212601	59544	38842994	C/G	0.44	0.46	0.675
rs2212602	59666	38843116	C/T	0.29	0.27	0.571
rs2226682	59913	38843363	A/T	0.38	0.33	0.127
rs2836512	66846	38850296	A/G	0.93	0.96	0.261
rs2836513	67245	38850695	G/T	0.23	0.22	0.692
rs1999328	67652	38851102	A/C	0.79	0.80	0.618
rs2212603	67955	38851405	A/G	0.73	0.74	0.676
rs3787919	67966	38851416	A/C			
rs2836514	68420	38851870	A/G	0.51	0.57	**0.044**
rs1023153	70226	38853676	A/G	0.09	0.09	0.699
rs1023372	70810	38854260	C/T	0.82	untyped	NA
rs2212604	72246	38855696	A/G	0.67	0.73	0.063
rs2226684	73330	38856780	G/T	0.82	0.82	0.992
rs2212605	73457	38856907	C/T	0.83	0.86	0.180
rs2187307	74389	38857839	A/G	0.14	0.13	0.901
rs3065412	74638	38858088	-/AA			
rs2898355	74640	38858090	A/C	0.95	0.93	0.442
rs2836518	75358	38858808	A/C	0.11	0.14	0.248
rs3838110	75952	38859402	-/G	0.65	0.68	0.399

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2836519	76098	38859548	A/G	0.59	0.64	0.134
rs3827207	77836	38861286	A/G	0.60	0.64	0.205
rs2836520	78449	38861899	A/C			
rs2836521	78507	38861957	G/T	0.08	0.09	0.765
rs2836522	80031	38863481	G/T	0.12	0.07	**0.033**
rs2836523	81695	38865145	C/T			
rs2836524	82775	38866225	A/G	0.05	0.04	0.539
rs2836525	82795	38866245	A/G	0.12	0.09	0.179
rs3833350	84611	38868061	-/C			
rs2836526	84657	38868107	C/T	0.83	0.85	0.536
rs2836527	84693	38868143	A/C	0.08	0.07	0.444
rs3834676	85020	38868470	-/T	0.79	0.82	0.270
rs2836528	85048	38868498	C/T	0.82	0.86	0.130
rs3761364	85100	38868550	C/T	0.08	0.05	0.132
rs2836529	85325	38868775	A/C	0.09	0.07	0.214
rs2836530	85452	38868902	C/T			
rs3761366	85868	38869318	A/G	0.07	0.04	0.259
rs2836531	85936	38869386	A/G	0.49	0.50	0.741
rs2836532	85990	38869440	A/T	0.30	0.30	0.921
rs2836533	86139	38869589	C/T	0.48	0.48	0.843
rs2836534	86497	38869947	C/T	0.86	0.89	0.374
rs2836535	87236	38870686	A/G	0.91	0.91	0.933
rs2836536	87248	38870698	C/T	0.86	0.86	0.945
rs3827208	87533	38870983	C/G	0.51	0.55	0.183
rs715860	87912	38871362	A/G	0.07	0.07	0.893
rs717231	88108	38871558	G/T	0.65	0.68	0.506
rs2836537	88494	38871944	A/C	0.43	0.39	0.251
rs2836538	89598	38873048	A/C			
rs2836539	90235	38873685	A/T	0.98	0.98	0.910
rs2836540	91287	38874737	G/T			
rs2836541	91359	38874809	C/T	0.09	0.06	0.324
rs2836542	92384	38875834	A/C	0.37	0.41	0.365
rs2836543	92410	38875860	C/T	0.54	0.55	0.863
rs881837	92900	38876350	C/T	0.30	0.28	0.673
rs3949052	94495	38877945	A/G			
rs2065307	94512	38877962	A/G			
rs3216105	97777	38881227	-/A	0.31	0.29	0.603
rs2073427	98333	38881783	C/T	0.09	0.06	0.249

TABLE 33

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2898353	231	38783681	A/T	0.22	0.21	0.629
rs960818	882	38784332	A/G	0.59	0.55	0.351
rs960819	960	38784410	A/C	0.12	0.01	
rs2410034	1194	38784644	A/C			
rs2836437	1530	38784980	A/G	0.14	0.14	0.989
rs2836438	1673	38785123	A/G	0.78	0.71	**0.047**
rs2836439	2096	38785546	C/T	0.72	0.68	0.265
rs2836440	2285	38785735	A/G	0.18	0.19	0.789
rs2226683	5873	38789323	C/T	0.80	0.77	0.342
rs2836441	7256	38790706	A/G	0.11	0.12	0.559
rs2836442	7988	38791438	A/G	0.32	0.28	0.269
rs2836443	8222	38791672	G/T	0.23	0.21	0.504

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2836444	8381	38791831	C/T	0.19	0.19	0.829
rs3787906	8814	38792264	C/T	0.97	untyped	
rs3838108	8915	38792365	-/C	0.58	0.55	0.526
rs2836445	9642	38793092	A/G	0.30	0.32	0.722
rs2836446	9902	38793352	A/T	0.11	0.14	0.425
rs3787908	10619	38794069	A/G			
rs2836447	10927	38794377	C/T	0.68	0.68	0.908
rs2836448	11032	38794482	C/T	0.11	0.14	0.302
rs2836450	14377	38797827	C/T	0.73	0.70	0.314
rs2836451	15608	38799058	C/T	0.93	0.94	0.499
rs1015022	15928	38799378	C/G	0.33	0.35	0.527
rs2836452	16296	38799746	A/G	0.17	0.18	0.750
rs2836453	17598	38801048	A/T	0.02	0.02	0.934
rs3787909	19272	38802722	A/G	0.05	0.04	0.546
rs2836454	20084	38803534	A/G	0.05	0.03	0.379
rs2836455	20577	38804027	A/T	0.17	0.15	0.472
rs2155718	28051	38811501	A/G	0.79	0.78	0.704
rs2836456	29466	38812916	A/G	0.97	0.94	0.174
rs2836457	29530	38812980	C/T			
rs2836458	29987	38813437	A/G	0.48	0.45	0.532
rs2032323	30012	38813462	C/T			
rs2051400	30322	38813772	G/T	0.04	0.02	0.476
rs2836459	32216	38815666	C/T	0.19	0.18	0.921
rs2836460	32516	38815966	C/T			
rs2836461	32544	38815994	A/G			
rs2836462	32746	38816196	A/G			
rs2836463	33137	38816587	G/T	0.68	0.68	0.988
rs2836464	33538	38816988	A/G	0.69	0.66	0.430
rs2836465	33798	38817248	C/T			
rs2836466	33802	38817252	A/C	0.39	0.39	0.948
rs2836467	33964	38817414	C/T			
rs3827204	34132	38817582	A/G	0.45	0.43	0.614
rs2836468	34210	38817660	C/T	0.12	0.12	0.879
rs3787911	34317	38817767	A/G	0.12	0.11	0.901
rs2836469	34499	38817949	C/T	0.38	0.39	0.914
rs2836470	34753	38818203	A/C	0.75	0.74	0.960
rs2212599	34845	38818295	C/T	0.71	0.64	0.095
rs2836472	35335	38818785	C/T	0.40	0.36	0.321
rs2836473	36423	38819873	C/T	0.56	0.53	0.433
rs1888469	36450	38819900	A/G	0.45	0.49	0.399
rs1888470	36481	38819931	G/T	0.16	0.19	0.356
rs2032322	38447	38821897	C/G	0.50	0.45	0.190
rs2410035	38784	38822234	C/T			
rs1573332	39387	38822837	A/T	0.58	0.56	0.554
rs2836474	39458	38822908	C/T	0.34	0.33	0.762
rs2836475	39822	38823272	C/G	0.15	0.14	0.817
rs3787914	40305	38823755	C/G	0.73	0.73	0.934
rs1888471	40869	38824319	C/T	0.28	0.27	0.760
rs1888472	40926	38824376	C/T	0.63	0.58	0.302
rs1888473	41010	38824460	C/T	0.63	0.62	0.683
rs1888474	41134	38824584	C/T	0.27	0.26	0.853
rs2836476	41984	38825434	A/G	0.46	0.45	0.838
rs3787916	42172	38825622	A/T	0.44	0.45	0.827
rs2836477	42753	38826203	G/T	0.94	0.95	0.505
rs970043	43011	38826461	C/T	0.04	0.04	0.848
rs2212600	43176	38826626	A/G			
rs2836478	43320	38826770	G/T	0.76	0.75	0.893

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2836479	43381	38826831	A/T	0.44	0.43	0.801
rs1475877	44142	38827592	A/G	0.35	0.33	0.450
rs2836480	44383	38827833	A/G	0.47	0.44	0.444
rs2836481	44726	38828176	C/T	0.41	0.41	0.999
rs2836483	45087	38828537	A/G	0.48	0.44	0.306
rs2836484	45141	38828591	C/T	0.46	0.46	0.939
rs2836485	45359	38828809	C/G	0.15	0.17	0.483
rs2836486	45421	38828871	C/T			
rs2836487	45456	38828906	C/T	NA	0.03	NA
rs1893199	45467	38828917	C/T	0.63	0.62	0.868
rs2836488	45486	38828936	C/T	0.23	0.22	0.913
rs1893200	45709	38829159	A/G	0.17	0.16	0.653
rs1893201	45716	38829166	A/G	0.85	0.85	0.947
rs2836489	47626	38831076	C/T	0.27	0.30	0.597
rs1888475	49413	38832863	A/G			
rs2836490	49796	38833246	C/T	0.94	0.91	0.196
rs2836491	49962	38833412	A/G	0.09	0.11	0.493
rs2836492	50075	38833525	C/T	0.20	0.21	0.669
rs2836493	50093	38833543	A/G	0.96	0.93	0.211
rs2836494	50571	38834021	C/T	0.70	0.69	0.697
rs2836495	50615	38834065	A/G	0.82	0.80	0.510
rs2898354	50780	38834230	A/G	0.27	0.26	0.846
rs3065390	50851	38834301	-/TA	0.11	0.10	0.936
rs2836496	51459	38834909	A/C	0.81	0.80	0.746
rs2836497	53193	38836643	C/T	0.66	0.64	0.756
rs2836498	53702	38837152	C/T	0.41	0.40	0.844
rs2836499	53736	38837186	A/C	0.32	0.30	0.567
rs2836500	53795	38837245	C/T			
rs2836501	54109	38837559	A/T	0.36	0.36	0.917
rs2836502	54126	38837576	C/T	0.31	0.32	0.738
rs2836503	54230	38837680	A/C	0.32	0.31	0.730
rs2836504	54894	38838344	C/T	0.52	0.50	0.620
rs3787917	55455	38838905	A/G	0.57	0.56	0.759
rs2836505	55499	38838949	A/G	0.74	0.74	0.982
rs2836506	56522	38839972	C/T	0.52	0.53	0.907
rs2836507	56662	38840112	C/T	0.51	0.52	0.785
rs2836508	56954	38840404	A/G	0.53	0.52	0.709
rs2836509	57267	38840717	A/G	0.35	0.33	0.453
rs2836510	58282	38841732	A/G	0.68	0.65	0.457
rs2836511	58916	38842366	A/C	0.32	0.31	0.832
rs2212601	59544	38842994	C/G	0.45	0.47	0.717
rs2212602	59666	38843116	C/T	0.30	0.30	0.994
rs2226682	59913	38843363	A/T	0.39	0.38	0.801
rs2836512	66846	38850296	A/G	0.94	0.91	0.184
rs2836513	67245	38850695	G/T	0.23	0.23	0.949
rs1999328	67652	38851102	A/C	0.80	0.77	0.487
rs2212603	67955	38851405	A/G	0.74	0.70	0.289
rs3787919	67966	38851416	A/C			
rs2836514	68420	38851870	A/G	0.53	0.49	0.363
rs1023153	70226	38853676	A/G	0.08	0.09	0.611
rs1023372	70810	38854260	C/T	0.84	0.81	0.315
rs2212604	72246	38855696	A/G	0.69	0.68	0.641
rs2226684	73330	38856780	G/T	0.85	0.81	0.216
rs2212605	73457	38856907	C/T	0.82	0.82	0.927
rs2187307	74389	38857839	A/G	0.12	0.13	0.685
rs3065412	74638	38858088	-/AA			
rs2898355	74640	38858090	A/C	0.96	0.96	0.893

dbSNP rs#	Position in SEQ ID NO: 4	Chromosome Position	A1/A2 Allele	F A2 Case AF	F A2 Control AF	F p-Value
rs2836518	75358	38858808	A/C	0.10	0.11	0.823
rs3838110	75952	38859402	-/G	0.68	0.65	0.457
rs2836519	76098	38859548	A/G	0.60	0.57	0.357
rs3827207	77836	38861286	A/G	0.64	0.61	0.449
rs2836520	78449	38861899	A/C			
rs2836521	78507	38861957	G/T	0.06	0.07	0.625
rs2836522	80031	38863481	G/T	0.09	0.10	0.810
rs2836523	81695	38865145	C/T			
rs2836524	82775	38866225	A/G	0.05	0.04	0.419
rs2836525	82795	38866245	A/G	0.10	0.14	0.132
rs3833350	84611	38868061	-/C			
rs2836526	84657	38868107	C/T	0.83	0.86	0.342
rs2836527	84693	38868143	A/C	0.08	0.11	0.209
rs3834676	85020	38868470	-/T	0.81	0.84	0.442
rs2836528	85048	38868498	C/T	0.86	0.88	0.350
rs3761364	85100	38868550	C/T	0.04	0.03	0.643
rs2836529	85325	38868775	A/C	0.08	0.06	0.271
rs2836530	85452	38868902	C/T			
rs3761366	85868	38869318	A/G	0.06	0.04	0.473
rs2836531	85936	38869386	A/G	0.49	0.49	0.915
rs2836532	85990	38869440	A/T	0.31	0.28	0.446
rs2836533	86139	38869589	C/T	0.47	0.48	0.810
rs2836534	86497	38869947	C/T	0.88	0.84	0.149
rs2836535	87236	38870686	A/G	0.94	0.92	0.378
rs2836536	87248	38870698	C/T	0.86	0.82	0.311
rs3827208	87533	38870983	C/G	0.51	0.49	0.598
rs715860	87912	38871362	A/G	0.09	0.11	0.463
rs717231	88108	38871558	G/T	0.65	0.67	0.588
rs2836537	88494	38871944	A/C	0.42	0.41	0.694
rs2836538	89598	38873048	A/C			
rs2836539	90235	38873685	A/T	0.97	0.97	0.749
rs2836540	91287	38874737	G/T			
rs2836541	91359	38874809	C/T	0.05	0.05	0.895
rs2836542	92384	38875834	A/C	0.34	0.34	0.998
rs2836543	92410	38875860	C/T	untyped	0.43	NA
rs881837	92900	38876350	C/T	0.29	0.28	0.811
rs3949052	94495	38877945	A/G			
rs2065307	94512	38877962	A/G			
rs3216105	97777	38881227	-/A	0.32	0.28	0.273
rs2073427	98333	38881783	C/T	0.08	0.07	0.700

[0256] Allelotyping results were considered particularly significant with a calculated p-value of less than or equal to 0.05 for allelotype results. These values are indicated in bold. The allelotyping p-values were plotted in Figure 1D for the discovery cohort. The position of each SNP on the chromosome is presented on the x-axis. The y-axis gives the negative logarithm (base 10) of the p-value comparing the estimated allele in the case group to that of the control group. The minor allele frequency of the control group for each SNP designated by an X or other symbol on the graphs in Figure 1D can be determined by consulting Table 31. For example, the left-most X on the left graph is at position 38783681. By proceeding down the Table from top to bottom and across the graphs from left to right the allele frequency associated with each symbol shown can be determined.

[0257] To aid the interpretation, multiple lines have been added to the graph. The broken horizontal lines are drawn at two common significance levels, 0.05 and 0.01. The vertical broken lines are drawn every 20kb to assist in the interpretation of distances between SNPs. Two other lines are drawn to expose linear trends in the association of SNPs to the disease. The light gray line (or generally bottom-most curve) is a nonlinear smoother through the data points on the graph using a local polynomial regression method (W.S. Cleveland, E. Grosse and W.M. Shyu (1992) Local regression models. Chapter 8 of Statistical Models in S eds J.M. Chambers and T.J. Hastie, Wadsworth & Brooks/Cole.). The black line provides a local test for excess statistical significance to identify regions of association. This was created by use of a 10kb sliding window with 1kb step sizes. Within each window, a chi-square goodness of fit test was applied to compare the proportion of SNPs that were significant at a test wise level of 0.01, to the proportion that would be expected by chance alone (0.05 for the methods used here). Resulting p-values that were less than 10^{-8} were truncated at that value.

[0258] Finally, the exons and introns of the genes in the covered region are plotted below each graph at the appropriate chromosomal positions. The gene boundary is indicated by the broken horizontal line. The exon positions are shown as thick, unbroken bars. An arrow is place at the 3' end of each gene to show the direction of transcription.

Example 8

In Vitro Production of Target Polypeptides

[0259] cDNA is cloned into a pIVEX 2.3-MCS vector (Roche Biochem) using a directional cloning method. A cDNA insert is prepared using PCR with forward and reverse primers having 5' restriction site tags (in frame) and 5-6 additional nucleotides in addition to 3' gene-specific portions, the latter of which is typically about twenty to about twenty-five base pairs in length. A Sal I restriction site is introduced by the forward primer and a Sma I restriction site is introduced by the reverse primer. The ends of PCR products are cut with the corresponding restriction enzymes (*i.e.*, Sal I and Sma I) and the products are gel-purified. The pIVEX 2.3-MCS vector is linearized using the same restriction enzymes, and the fragment with the correct sized fragment is isolated by gel-purification. Purified PCR product is ligated into the linearized pIVEX 2.3-MCS vector and *E. coli* cells transformed for plasmid amplification. The newly constructed expression vector is verified by restriction mapping and used for protein production.

[0260] *E. coli* lysate is reconstituted with 0.25 ml of Reconstitution Buffer, the Reaction Mix is reconstituted with 0.8 ml of Reconstitution Buffer; the Feeding Mix is reconstituted with 10.5 ml of Reconstitution Buffer; and the Energy Mix is reconstituted with 0.6 ml of Reconstitution Buffer. 0.5 ml of the Energy Mix was added to the Feeding Mix to obtain the Feeding Solution. 0.75 ml of Reaction Mix, 50 µl of Energy Mix, and 10 µg of the template DNA is added to the *E. coli* lysate.

[0261] Using the reaction device (Roche Biochem), 1 ml of the Reaction Solution is loaded into the reaction compartment. The reaction device is turned upside-down and 10 ml of the Feeding Solution is loaded into the feeding compartment. All lids are closed and the reaction device is loaded into the RTS500 instrument. The instrument is run at 30°C for 24 hours with a stir bar speed of 150 rpm. The pIVEX 2.3 MCS vector includes a nucleotide sequence that encodes six consecutive histidine amino acids on the C-terminal end of the target polypeptide for the purpose of protein purification. Target polypeptide is purified by contacting the contents of reaction device with resin modified with Ni^{2+} ions. Target polypeptide is eluted from the resin with a solution containing free Ni^{2+} ions.

Example 9

Cellular Production of Target Polypeptides

[0262] Nucleic acids are cloned into DNA plasmids having phage recombination cites and target polypeptides are expressed therefrom in a variety of host cells. Alpha phage genomic DNA contains short sequences known as attP sites, and *E. coli* genomic DNA contains unique, short sequences known as attB sites. These regions share homology, allowing for integration of phage DNA into *E. coli* via directional, site-specific recombination using the phage protein Int and the *E. coli* protein IHF. Integration produces two new att sites, L and R, which flank the inserted prophage DNA. Phage excision from *E. coli* genomic DNA can also be accomplished using these two proteins with the addition of a second phage protein, Xis. DNA vectors have been produced where the integration/excision process is modified to allow for the directional integration or excision of a target DNA fragment into a backbone vector in a rapid *in vitro* reaction (Gateway™ Technology (Invitrogen, Inc.)).

[0263] A first step is to transfer the nucleic acid insert into a shuttle vector that contains attL sites surrounding the negative selection gene, ccdB (*e.g.* pENTER vector, Invitrogen, Inc.). This transfer process is accomplished by digesting the nucleic acid from a DNA vector used for sequencing, and to ligate it into the multicloning site of the shuttle vector, which will place it between the two attL sites while removing the negative selection gene ccdB. A second method is to amplify the nucleic acid by the polymerase chain reaction (PCR) with primers containing attB sites. The amplified fragment then is integrated into the shuttle vector using Int and IHF. A third method is to utilize a topoisomerase-mediated process, in which the nucleic acid is amplified via PCR using gene-specific primers with the 5' upstream primer containing an additional CACC sequence (*e.g.*, TOPO® expression kit (Invitrogen, Inc.)). In conjunction with Topoisomerase I, the PCR amplified fragment can be cloned into the shuttle vector via the attL sites in the correct orientation.

[0264] Once the nucleic acid is transferred into the shuttle vector, it can be cloned into an expression vector having attR sites. Several vectors containing attR sites for expression of target polypeptide as a

native polypeptide, N-fusion polypeptide, and C-fusion polypeptides are commercially available (*e.g.*, pDEST (Invitrogen, Inc.)), and any vector can be converted into an expression vector for receiving a nucleic acid from the shuttle vector by introducing an insert having an attR site flanked by an antibiotic resistant gene for selection using the standard methods described above. Transfer of the nucleic acid from the shuttle vector is accomplished by directional recombination using Int, IHF, and Xis (LR clonase). Then the desired sequence can be transferred to an expression vector by carrying out a one hour incubation at room temperature with Int, IHF, and Xis, a ten minute incubation at 37°C with proteinase K, transforming bacteria and allowing expression for one hour, and then plating on selective media. Generally, 90% cloning efficiency is achieved by this method. Examples of expression vectors are pDEST 14 bacterial expression vector with att7 promoter, pDEST 15 bacterial expression vector with a T7 promoter and a N-terminal GST tag, pDEST 17 bacterial vector with a T7 promoter and a N-terminal polyhistidine affinity tag, and pDEST 12.2 mammalian expression vector with a CMV promoter and neo resistance gene. These expression vectors or others like them are transformed or transfected into cells for expression of the target polypeptide or polypeptide variants. These expression vectors are often transfected, for example, into murine-transformed a adipocyte cell line 3T3-L1, (ATCC), human embryonic kidney cell line 293, and rat cardiomyocyte cell line H9C2.

[0265] Modifications may be made to the foregoing without departing from the basic aspects of the invention. Although the invention has been described in substantial detail with reference to one or more specific embodiments, those of skill in the art will recognize that changes may be made to the embodiments specifically disclosed in this application, yet these modifications and improvements are within the scope and spirit of the invention, as set forth in the claims which follow. All publications or patent documents cited in this specification are incorporated herein by reference as if each such publication or document was specifically and individually indicated to be incorporated herein by reference.

[0266] Citation of the above publications or documents is not intended as an admission that any of the foregoing is pertinent prior art, nor does it constitute any admission as to the contents or date of these publications or documents. U.S. patents and other publications referenced herein are hereby incorporated by reference.

Nucleotide and Amino Acid Sequence Embodiments

[0267] Table A includes information pertaining to the incident polymorphic variant associated with osteoarthritis identified herein. Public information pertaining to the polymorphism and the genomic sequence that includes the polymorphism are indicated. The genomic sequences identified in Table A may be accessed at the http address www.ncbi.nih.gov/entrez/query.fcgi, for example, by using the publicly available SNP reference number (*e.g.*, rs756519). The chromosome position refers to the

position of the SNP within NCBI's Genome Build 34, which may be accessed at the following http address: www.ncbi.nlm.nih.gov/mapview/map_search.cgi?chr=hum_chr.inf&query=. The "Contig Position" provided in Table A corresponds to a nucleotide position set forth in the contig sequence (see "Contig Accession No."), and designates the polymorphic site corresponding to the SNP reference number. The sequence containing the polymorphisms also may be referenced by the "Nucleotide Accession No." set forth in Table A. The "Sequence Identification" corresponds to cDNA sequence that encodes associated target polypeptides (*e.g.*, ELP3). The position of the SNP within the cDNA sequence is provided in the "Sequence Position" column of Table A. If the SNP falls within an exon, the corresponding amino acid position (and amino acid change, if applicable) is provided as well. Also, the allelic variation at the polymorphic site and the allelic variant identified as associated with osteoarthritis is specified in Table A. All nucleotide and polypeptide sequences referenced and accessed by the parameters set forth in Table A are incorporated herein by reference.

Table A

RS_ID	Chrom-osome	Chrom Position	Contig Accession No. [1]	Contig Position	Nucleotide Accession No. [2]	Sequence Position	Amino Acid Posi-tion	Locus	Locus ID	A [3]	Allelic Variability	OA Assoc. Allele
rs756519	6	170707371	Hs6_7740_34:11	520890	NM_002793	intron		PSMB1	5689	F	[C/T]	T
rs1042327	6	does not map			NM_003194	exonic		TBP	6908	R	[T/C]	C
rs8770	6	170743040	Hs6_7740_34:11	556559	NM_002598	mma-utr		PDCD2	5134	R	[C/T]	C
rs1563055	8	27976377	Hs8_23822_34:16	6328752	NM_018091	intron		ELP3	55140	F	[C/T]	T
rs912428	13	44965904	Hs13_24680_34:1	28147904	NM_015116	intron		CHDC1	23143	R	[T/C]	T
rs1888475	21	38832863	Hs21_11669_34:9	25572863	NM_004449	intron		ERG	2078	F	[A/G]	A

[1] Contig Accession Number which can be found in the NCBI Database:
ttp address: www.ncbi.nih.gov/entrez/query.fcgi

[2] Sequence Identification or Nucleotide Accession Number which can be found in the NCBI Database:
http address: www.ncbi.nih.gov/entrez/query.fcgi

[3] "A" column is the sequence orientation ("F" is forward, "R" is reverse).

[0268] Following are genomic nucleotide sequences for a *chrom 6* region (SEQ ID NO: 1), an *ELP3* region (SEQ ID NO: 2), a *CHDC1* region (SEQ ID NO: 3) and an *ERG* region (SEQ ID NO: 4). The following nucleotide representations are used throughout: "A" or "a" is adenosine, adenine, or adenylic acid; "C" or "c" is cytidine, cytosine, or cytidylic acid; "G" or "g" is guanosine, guanine, or guanylic acid; "T" or "t" is thymidine, thymine, or thymidylic acid; and "I" or "i" is inosine, hypoxanthine, or inosinic acid. Exons are indicated in italicized lower case type, introns are depicted in normal text lower case

type, and polymorphic sites are depicted in bold upper case type. SNPs are designated by the following convention: "R" represents A or G, "M" represents A or C; "W" represents A or T; "Y" represents C or T; "S" represents C or G; "K" represents G or T; "V" represents A, C or G; "H" represents A, C, or T; "D" represents A, G, or T; "B" represents C, G, or T; and "N" represents A, G, C, or T.

chrom 6 genomic sequence (SEQ ID NO: 1)

>6:170689051-170779900

```
1       tggcctagcc caggccatct gccacacttg catagaatgt ttttcctatg gaagcttatt
61      ttggaatata atcacagagg aaattgagat aaacaggctt ttccttttct ggacaattct
121     tagagataaa atctactgca gaaggcaaga cacttaactt ctgcccagaa actgatgtca
181     cgtggttaac gtgtggtggc cacatcaact gaagccgaca gtgacaccRa gtcagcatcc
241     tgggtgcagc tgccaccctg tcactctcat cacattccac cattcccagg ccacagaggc
301     aagaggatac tctcaaaact tagagatagc tttagtttta ggaaaatagg acggaaaaat
361     atcttatgcc tcagaataat aggtggaatt caattgctct tcaaggcagc acaagcataa
421     tgtccaaata ggctttacaaa ggctttccct agattgtggg tgattgatct gtggcaggct
481     attaagggaa gttcaggatg gccaggctat tttgaggctg atatcttgga gaaccctctc
541     tctctcctgc aaaccactcc cttggcatca ctctcagaga caagctgctg gctgtgcaag
601     cccacaccct gactcagggt ggcatttttc tcaagccctc tcctttaag gccatcaggg
661     atctgagccc ccatgggtag ggaacaggcc aggcagctgg agcgtacaag agtcaccact
721     acgaatagct tgactctgaa gtttctaaaa gggaacctgg accacctgag cctccccaga
781     agacgcctca gtcacattta ccctgctgct gccattagta tcaggcagag ccatctgtac
841     acgcgggaac atgaaggcca ctttgcaaga cttcagctgg tgggttaaat gtggctcaca
901     gctgtcgctg aggcacactc cccaaaatag tctcaacaca gcagtaggaa agatgacaca
961     gaggtgactg agactaatag caatacagta ttactattat cccttgaata aagtatgtaa
1021    atcaaggtgt taaccatcag gagcagagaa aagagagtgt taagtatagg ggcttagctg
1081    taaaaagaat cagaagaaaa agaaaaaaaa accctcagtt aaagggctag atagtctaga
1141    aaatttgtta ggtatttata ttattaacac agagcagggt aacacgatag aatagaaacc
1201    tgttacaaac aggcaacaac aacacaaaa tagacaacaa ccctagaaga aaaatgcctt
1261    gaaggaaaag ctggaatact gtgagagact taccagtggc ctgtctgcgt gtaactaact
1321    cctcatcccg acttggtcac gcaaaggaca ggtgaccata cctccagaga ggtggaaagg
1381    ggccctacat gagtgagagg ctcaagtcct gcccaagtgg aatctgtgat tctgtgatct
1441    aaagaaagtt tgtggctatt tttagaaact aaagtttatc tcatattgac acaaactcaa
1501    aaatcaatga tactttgaga tatgtcatat cacaaaaaag atttctcctc tagtacatta
1561    tcatttaacc aatacaaaca ggtctgggcc aggtgctgtg gttcatgcct ataaacccag
1621    cactttgaga ggctgagggg ggtggatccc tagagcccag gagtttcagg ccagcctggg
1681    caacatggtg aaactctgtc tctaccaaaa gtacaaaaat tagccaggta tagtggcaca
1741    cacctgtagt tccagctact aaggaggcta aggtgagagg accactgagc ccagggacgt
1801    agagactacg gtgagacatg attataccac tgcactccag cctgggcaac agagggagac
1861    cttctctcaa aaagaaaaga aaagaaaaag aaacaggtct aatttgttca tctaagcaat
1921    gataagattt atatgaacat aagttgcttt attgatgaaa aattgaacat aatctaatca
1981    agcctctaaa tttaactgcc aatttatagg aaaagacagg acagaaccta caggaatgca
2041    atcatttata tctagaatgt ggaagattct gcatgacaaa cgacttggat tcttcaacat
2101    gtaaatttca aggaaagaga gagaggagga gataaaaagg cttgttccca gatttgaatg
2161    acatgttaat agacatttat gagacaatca aggaaatttg aacatggact gcatattgaa
2221    tgttgaggga ttatagttaa tttttaaagg tacaattgtg atactgtgat tatatttta
2281    aatgcgatca ttatctttta ggagcactaa aatatttact aataaaatta taggatttac
2341    ttcaaaataa acaacgataa taagattacc atgaatagtg gtgggtgaaa tatacaaggg
2401    gcttatttga catttccata ataaaaaaca cgaatgaata acaaagcatt atagaaattc
2461    aagtaaaaaa tagctcgtgc ttagtaataa atcaaagcgt gctggacact ttaaataata
2521    aacaaagata agatcttgcc ctctagaaaa cagctctaat tcaggacaga cttgctcaca
2581    tcagatggaa gagtcagaat gagatgtgct gagtagaagg tagaacggtc gctagcagag
2641    ggtgggaagg tggtatgtgt gggggagagg agaaagagag gttgattaat gggtacaaac
2701    agacagttag atggaaggag tgagatctgt tgttcgacag tagagtaggg tgactacagt
2761    taacaacaat atttgcatat ttcaaaatag ctagaagaca ggacttggaa tgttcccaac
2821    acatagaaag gtgatgaact caaggtgctg aacacccaaa atacccctgac ttgatcatta
2881    tgcaataaca aaatatcaca tgtaccctgt aaatatgtac aaatactaca tatcaattta
2941    aaaattttca cacaagaatg agatgtgctg atgcatgtgg aggccctagc tccagactgg
3001    gtgtaaactt caagccactg aagatcttat ttccaaggtt tttctacttt gaaattccaa
```

3061 acttatttt ctagcagatt tataagggac acgggacaac ataaacttgt taaagtgaca
3121 agagaaagta aatatgccct taaatttata ccaaatcttc tgacaagtct tgactgataa
3181 ttgtttcctt caaatttgtg aaaaacatga gagaaaacgt gtttgtatct catttttaag
3241 tgtggacact tggcattgct cacggcttcc aacggaataa aatagggctt agttgttttc
3301 cattagcttt ttcctttgtg tgtgtgtgtg tgtgtgtgtg tgtgtgtgtg tgttgtgtgt
3361 acatattggc tctaagcatt tattagccca ataattttta gtgaaactct ccacttctca
3421 atatcttttg ccgtattaga tttttgtaac atgtgctaaa ggttaaaaca ccttttcccc
3481 ttcatgaagc ctgagagaag tcggtttttct gggttttctc aagacaaccc agaggttttg
3541 tatacgtctg tctaaaaagt ctcagatttt tcttgctaat tgtgcacctt cataatcaag
3601 cagacaaatc agaatattat tttggtgagg ccatcatcta aactaacagt ctttatgtac
3661 agaagcagca ctgaccgggt tcatactcct cagttagcaa gtcaacatct tcctcctgcc
3721 agcaacccat cccagaatat ctgtggctta ttaatactta tgaaaacaac agtcttcatt
3781 atttactaat taggagatga tcagatgtat ctattgatag caacaggcta tttaaaagtg
3841 aaataatcta tcaaacagat tttttatcaa ctcaaagttt ccagttagat atttttcatt
3901 aaattgattg ctagattgca gccacaatca aacttaagta ttataagaag tttggttggt
3961 cttttaaaat catgcaaaaa ttcaaggggt gctattaaat atagaattcc aaatgtataa
4021 agtcttgtcc taaaatggtc aataaaatga accagtccac tggttcattt ataggggggcc
4081 agtccactac attaatttgg atgttcttcg tctgcatttt catgttttca cacacctgca
4141 gtcattgtgt acaattctgg actcttgatt ttcatttagc attctgcgtt aatattctga
4201 catgttgctg ccaggtcttc atggccacca cttttaatgg ccagaaaata tttcatgtag
4261 tgaacatttc ataaattact taaccatgtc ccaattattg gttatttaag gaatttaaaa
4321 ctaaaacacc actcttgtga caaagttctg atgtatccag atgtactcat gccaagtcgt
4381 ccatcaatag ttctgctaaa ccctgtcaga gcccttttct gaagggaacc aggaaacatc
4441 tcacaacaag aagcttaagg cctctacaaa atgacttcag ggttaggatt tcaatttcac
4501 tctgaggcac atacaggaac cactaggtta tttggcttag aatggaggga agtgtcattt
4561 tgtttctgtt cggcctgcag gaagctcctt cccaggccct gcattgccaa ttgaacaatt
4621 gaacaattct cattgttcaa ttcccaccta tgagtgagaa catgcattgt ttggtttcct
4681 gtccttgcga tagtttactg agaatgatgg tttccagctt catccatgtc cctacgaagg
4741 acatgaactc atcatttttt atggctgcat agtattccat ggtgtatatg tgccacattt
4801 tcttaatcca gtctatcact gatggacatt tgggttggtt ccaagtcttt gctattgtga
4861 atagtaccgc aataaacata cgtgtgcatg tgtctttata gtgcctagaa cataatagga
4921 gctccagaaa tactgttgaa aaaatgaata aattgagcac actaagtgtc tgaataaaat
4981 accctgacca taccccctaaa taaacaacat aaataagcaa atttcaattt ctcggaaaag
5041 ttatatttta gtgtccaatg ctcttgttat gcagtaatgg catctttgat tattcatatt
5101 cgttagagct tccagaaagg agtattgcaa atcacacggg cctctgactc tcatgaccaa
5161 atccccctgt cactgtcctt gttctctgat ccttcctctg ggccctcgga aatgctggtc
5221 tccatcaaat tgctgtaaac agttttcaga aaaagttctc tttgggaagt ttcaagagaa
5281 aaccacaaat ttcctggaaa tgcttcatgc ttcatgacat ttaaggcttt cagagccttg
5341 aacttcagga gcaagatagc tggtaggtct tctggaggtc ttgcctaacc tgagaaggtc
5401 ccagagaatt tgtgcataga acctcccagg aagcagtaag acaggctggt gcagtcccac
5461 aggatgagaa aggtaagagc ttaccaatgt ctccagtttt gtaaatgaat gttcttagca
5521 tttttggtga ggagaaaaaa atatcaaacc catcacagac agatcagcag tctcttgacc
5581 taggtcactc aaggggttct caacaatcaa ttctaaaatg caagtgaaaa atgtcaatat
5641 aaggctagac acaggggctc atgcctgtaa ttccaacact ttggaaggcc aaggcagacc
5701 tagaactttg taaatctgag atttgctcc atgactttgt ggatactttc tactaatacc
5761 acctacacaa aatcttcaac caagaatctt aattgcattt atcaacttgt gtccttagat
5821 cataacattt agattcattt gaaagaaatt tattgaagta aaagaaataa gaagaacttg
5881 atagcacaaa acaaagaaaa cccagaaaga gagagagaga gagaagcaga aaaactaaac
5941 actgaaaccc agagagagag agagaagtag aaaaactaaa cactgagtct taatctgttc
6001 tgccactagt cagcagcctg cacagagcac tttaatgtat tctctgtcca ttagtttcct
6061 tgtttatgaa agtatatagc tccaaaaaaa ttctgtgttc tgatttttgt ctctccaaac
6121 cacaaccagt cccctgctcc cttctctcct cctcctcctc cttcttcttc tttctctctc
6181 tctccctgtc tctctctctc tctctctctc tccccctttc cctctccccc acccacccac
6241 ctcccaaccc ctgcatacac ctaggacacc tccagcatag gttactacca attttgcaca
6301 cctccagcaY aggttactac caattttgct gggtttatct ccttctgtcc tttccgcttt
6361 gatctgagga atagctgaga tttaggacag caacaaggtg tacctccttc caggttataa
6421 aacaggatta atgattaggc tcaaggcccc ttcctagtca ctcagtaaag tctgtgcact
6481 ggaaaactgt ggtagcagtt ttctgagcat tagaaaactg tggttctcac agaggctgga
6541 tgagtcaaca ctgccatctg gcggcctctt ggagggtgat gtggagcctg gctttcattg
6601 aagaatgaag gtcccttgat ttcctgaccc tcagccaact ctccagcagc ttctcactgc
6661 agaagaggtc aggccattgg tcagcttgag gacaaagtgg gaggatcaca ctttcgatca
6721 cctatacttt ctaacaatca gccctgtgga catctgctca cgccccatgc tgtttttaaa
6781 atattttccc attatagaaa tatttttcaa agatgattca caagctccag gagccattca
6841 gacaagggag agcaaattgg cagctaaact cattcaagag tggagcagat gcacatgaag

```
6901  ctctgtctgg cggaggaggc acaagacacc gagcctggct gggagggtgc tcatgacaag
6961  agtggggcca caggcctctc ctttcattgg acatagtggc catacaaagt ggctgccttg
7021  aaatgcaccc acatacacta tcggtcctcc cggtctaggg agaaaactgg cacagtatgt
7081  caacagataa atcagcgcaa tcctgtgggt gaagcagtgc acccatactc ttcattctgc
7141  tgagcggaac tcaagggtga gacacttgta ttcctaactc cacttgcctt caggctcctc
7201  caacattcca aattgcccat ggacagagct actacccctc catagaagtg acaacttgaa
7261  ataaaagatt tgaagctcct tcccacgttt agacccaggc ctgctgctag gaactccaga
7321  ggagggatgg aaagaagttt gcactgctca cagatttaat gtttctctca caaccagaag
7381  taggcagcag gatggatttt caatcaacac taacaaacgg atcactcctg ggtcctttaa
7441  acaagttcca tgtctctttа taggttttag gtgcctccta tgtgttcaga cttcgtataa
7501  tggatatata agaaaagtaa atgggagggg caatatttaa gaaataacag caaacaattg
7561  cattcatatt taatataaac tacaagtatc aagttaatag acgctcagaa gaaattcata
7621  aaatctagaa aagttgggaa aatctcaata gagaaaataa aacttgatct ggacttтaag
7681  agtatgatтt ataaagttca agcggacagt acacaaggtc agacaatgtt agctgaatca
7741  ctgaagaatg agaatatcac acccactтaa caaagcagcc cagctagtta aagaagtatg
7801  ttgaagaggt agggagttgg gtgggggagg cgaggatggc gtggagggat ctgaaaacta
7861  tcaaccttaa ataatgagat ttagaaaata tgattaagta gagggttaat tcgagtgcag
7921  agcttgagaa tggccacctg gaaacactga ctctaaacca gtaaggttaa tgtttcaaag
7981  tggagaagtt aaggtttcac ttagaaattt tagcaggatc acattttcca tcaagacca
8041  gtgcattcgc cacagcaatt tgattggtta tagattgctg ctcattccaa gattacttta
8101  ttactctgtg cggaggagta gtgatttgag gggtcttatg tctggtgcct ttttgtcttg
8161  tttacagggg aaaaggcaga agttgcgcct gcatgccgca taactcaggc tctgcatagc
8221  cacatgtctt tcaaggctca gaataatttg aagttccaac agcttaagt ttgaattaat
8281  ttcacaaagc ggagaaagac ttggacttcg tgcagtaatg aagaccaccg atgggtactg
8341  aacagctctg gtgggtttgc actcagagaa aggagcctaa gatgcagaag gtgcagtgag
8401  gcagcagcca tctgctcttg tgctgcctga cagagcatga tgggctgtca ccgctcacgc
8461  gtgttcttta cctgctgact cacctggcgg catgggctgc atatggggtc ccagctcctt
8521  aagctcctgt caggcccttc tgcaacttct cccaagctct tgggccaggt gcatgtctag
8581  ccatgaaaaa ggaggccagt acctgatcac taagtgaaag ttctaaggta gtgggactgc
8641  cacaggtgtc ccccatggtc ccaggtcaca atccagtctg ttgaccctcc tccttttgca
8701  ccatcgcccc tttgacagcc tgtgctatgg gttttaggct cctagcacca aacagaaaca
8761  ggcttatata gatcatctaa tcagctcttc ttatgtgagg ccgaactctg taataaatct
8821  ttttatgtct cctagggctt ctctgattga acctgtctga tgaggagtta aagaagttct
8881  caaattgtgt atgcataaga atcacctggg atttctagct cagagactgg gacaatаggt
8941  ctattgaacc taggagttca ttttgaacaa gtgctctacg taattctgat acagggaatc
9001  ttccagttac agtttgaaat tcacaaatac aagggatgag agacctagaa tcagaaagca
9061  tgttaataca cttttgggcc attaagtgct cacccaggta acaggtacag aaaggcagaa
9121  aaaggaaacc tatcagggta ataattatgc ctttttttttt ttttttttтt gagacagggt
9181  cttgctctat cacccaggct ggagtgcagt ggcacaacca cagctcactg cagcctтgac
9241  ctcctgggct caagtgattc ttccagttca gcctcttgag taactacgac tacaggcatg
9301  tgccaccatc cctggctcat tttttgtaga gagggggttt ggccatgctg cacaggctgg
9361  tctcaaattc ctgggctcat gtgatttccc cacctcagcc tcctaaagta ttaggattac
9421  aggcgtaagc cactgtgctt ggccaagaca ttttggtaag aaatattatt ttcctactaa
9481  attgtctaca ttccccttgg gtaggcttgc aaagtcactg tgactacagc aggagctatt
9541  gctgcatggg aaatatggag acacgagtgg tacctggcag tcacgggctc agtttgtttc
9601  taacctccca agtcagcaca gccccactga gcagactgcc ggaaagtatt tatgccatct
9661  gtcggataat tagacaaatc ccaacatctt acgtgcattc tgtgtgtata aatggagtca
9721  tggccaacct ttcaatgcag tttccatcaa tcacttgtaa tatcaccaga tacttccaat
9781  ccccttgcag gcagtaatga agagaaagtc tctacatcag cagcttctca ctggaatctt
9841  caagcctaac tcttaagaat gaatcatact tctaatgttt atcaaaggtt ttcttttcac
9901  acaaggaatg tgcctgaatg atctataaaa ctacccaaat aactagtagc caggttagct
9961  ctaggagcca tatgccaaac acattctgga ctaagtcgtg ttcactccaa aactaagacc
10021 atgttcaaag tctacagcaa tactggatta aaacaatgtt agctgaaggt tgtaaaaaaa
10081 catcatggaa cactaattat gtgccatcaa tcattactca atttgtagaa cttccctata
10141 caccttggga ggtgagaacc ttatagaaaa tcctagatac acaacttтat ataaacagaa
10201 aattccaaaa tgggaaatcc tttagaataa gaatatacct agtgtatata aagaagaaaa
10261 aatgtagatt tgaaattggg atactctaca gtttttagtt gggacattgg gatagttaat
10321 tttaggtgtc aacttgactg gattaaagga tatcaagaca gcaggtaaag cattacttct
10381 gggtttgtct gtaggagatgt ttccggagac tggcctagga gtttgtggac tgagtgcaga
10441 tcagcctgtg tgagcaggca ccatccaact gaatggagcc cagatagaac caaaaggcaa
10501 aggcaaatca ttcactgtct ttctcctcga gccagggact tgattagcaa cccctcacac
10561 ccaactcctt attttcagga cttcaagggt tataccatca gcttccctgg ttgtgaggcc
10621 ttcagacttg gactgagcca tgctgccagt ttctctggct ccccagcttg cagacagcca
10681 ggcatgggaa ttctcagtct caataactga gtgagccaat ttctttaata aacccttttct
```

10741 catctctctc tatatacaaa catatcctat tggttctgag tctttggaga atcctcatac
10801 agacactgtt aagagatgaa ccaggtgtta ccactgtgtc cccaatgcct gggatagtga
10861 gtgacagtat tgatgtttgt gcaataaatg tttacaatgt gtatctacta gcagctttcg
10921 ataatttgaa ttatttataa aaggcaaaat aaacaaaagt ggtatctaag attaaccact
10981 aacttagtaa aattccattt ataccacagg ttgttctggt acaaagcata caataactcc
11041 catgttacat ataatttgac ttgttcaata acaagaaaat tactcaaata ttataatgga
11101 gttaaaatgt atttaataga tctaaaaaat tttggctcta tcaaaactta ggtctcaatt
11161 ataacattac taaagtgctt gtaaaaatta tcccagattt ctggctacag cttgtataaa
11221 ggcctatttt tttttttta cagttttatt ttggttgaag atttttctcc aaaatagcta
11281 ttccagatgg cttaacagtc ccagaagtga aaaatcttaa gatatttcat ttataaccat
11341 tagagtctta ataaaaccct agtaaatact ctcccttctg gatggtttaa aggtcccttc
11401 aggcaagctg gctgcgtaaa caccagagcc ctcttcataa gataagtttg ctcaaaaggt
11461 caacttttac agagaaattc ctacctcatt agtgtaaggg aaaattaaca tgacctgttt
11521 tcattactta aaatgcaaaa aaaaaaaaaa aaaaaaaaaa aaaatctcag aaaaatagaa
11581 aagggtggga aaaatgaaga aaattaaaag aaattctact tcctatatct gtcctgctta
11641 gagaagacaa gttatagcaa aatgagtact tcaggtttct cttttaataa acaaaaccat
11701 ccaaggtaca gttccaaagt acaaaatcaa ccaggtctga actgattggt gataagagca
11761 cacagatcag tccttcctta aggaaacagt ttcctccctg atgccctctt tggtcactat
11821 gcagatccgg agtgcgtccM cagtgtacac atctctctca gccgcagaaW tgaagacatc
11881 tttcaccagc cgcatggctc tgtccaagga cagcggaaca tgctccacat tctgcatgtt
11941 cttaaaacca acctggtggg acatgaaact tgggtgagat gtcatgtgac agtgagcaca
12001 aaggaaaggt tcaagtttct tccaataccc tcatgtgtac gaggatttgt gatgaaaata
12061 ctaYacaaaa ttaaaatgtc cttcagactg aataaagacc cttccagacc tggatgaatt
12121 acacacatca gaaatctgac aacgattccc tggcaaagct cccactcttg agaagcacat
12181 gacccggaga ggtggacgta tgcaagcaaa gtgatcagag aattgctata actaagaaga
12241 aaataagagc caggagagcc ccaacagatg tccactaagt ctcctagaag aagacaggct
12301 tcagcagaaa ggacttttaa gtaggtgagc gctgaaggct acactgaaga gcacagaaca
12361 ttccagactg aagatgtggg acggagttag gaaaagcaca tcttttctga gaaaagcaga
12421 gttagggtct gggtgtagtg gggtgacagg agatgaggtc aataagcaat aagcagagga
12481 gtagctatat atgacatcct tcagaaaact gagcaggagg aattagggaa gtaaacttgt
12541 aggcagaaag gatgttagga aataaatcca ataatctaat aatgtaggtc tgaatttagc
12601 cagcagtaat cacaaagagg gacgaattag aaatacaggc ggcctttgaa taacaccgtt
12661 ttcaaccact caggcccact gacacataaa ttttcagtaa acacactgag aagtttttgg
12721 agactcgcaa cactttgaaa aactcagatg agccaagtag cctaaaaata ccttaaaaat
12781 taagagaaag gtatgccaca aatgtataaa ctatatgtag atactagcta ttttatcatt
12841 tactaccata aaatacacat aaactgatta taaaaagtta aagtgatctc tcaatgttct
12901 cctttgtttt tcattgtgtt tagtgcgatt attataaacc ttaaataaca agtggcccaa
12961 acaaagcact attagtgatg ctggaactgc tccccaagaa gcagggaaag ttatgacatc
13021 acaagaaaaa gctgaattgc ttgatatgta ctgtagattg aggtctgcag ctgtggttgt
13081 ccaccactcc agacagatga ttctccttgt aaacagatga tgtaaactta cagtatcaac
13141 aaatacagta ttgtaaatgt attttctctt cctataattt tcttaataac attctctttc
13201 ctgtagttta tttatcataa gaatacagca cataatacat atgtaaaata cgtgataatc
13261 cacagtttac attattggca aggcttccag tcaacagtag gcttatttgt aagttttctt
13321 ggagtcgaaa gttatatgtg gattttccag tgctcgggga actggcgccc caatccccgt
13381 gttgttcaag gStcaactgt atgcttggga gttcaagtac agtattgggt aacacagaaa
13441 gggggggtaa gagggaaaaa ggcattttta tgatcttcag gtaaagacag caagagaatt
13501 agccactaca gacataaaag agttggaagc catgagaata caggaaaaca atcaaaacca
13561 tgggagtagg taaggaccca caagagagta ggcagaacac agagagagac catgaggttt
13621 ctgtaggaca cgtctgccaa actcaaacag taatttataa gaaagtcttt atatcttggc
13681 tctcctaagc taatgaagag gagaacttgg aggaaggcac ttcaactgaa caccatgaca
13741 agttggacat agtatcatta cctggacaca gtatcattac ctggttgtca agcaggggct
13801 gtagcatggc acttgctgag cctccagcct tgaaggagtc tctctggtaa gaccctactg
13861 gatcaaagct gtatacagcc cccttttcctt aaagaagaaa acagtattca taaggatggt
13921 atccaatcac aatcccaaat catcgcaaaa ataaatcagg tcaaaacgtg acacaaaacg
13981 gactatcacc ttggctaaaa cttcagggaa cagttggaac acagccactg ttgcactggt
14041 gacagctgca gcacacacac tgttgcacat gtgacagcca gaacccagtc accattgcac
14101 aggtgccacc cagcagacag ccccaatccc cgtgttggtg tgttgttcaa gggtaaactg
14161 taggcttggg agttaaaata caatattgag taacacagaa agggtgggta agagggagaa
14221 aggcattttt atgatcttca ggtaaagatg acaagagaat taaccactgc agatgtaaaa
14281 cagttggaag ccatgagaat acacaaaaat aatccaagcc atggtagtag gtaaggaccc
14341 gtaagagagt agggagaaca cagagagaga tggtgaggtt tctgtaggac acatcagcca
14401 aactcaaaca gtcatttgta agaaagtctt tatttcttgg ctctcctaag ctaacgaaga
14461 ggagaacttg aaggaaagca cgacttatgt atatagacag gtccaaggga cacatccgca
14521 agacacagta aaacgaagag aattctgtaa cctgtaaaat acgatactgc ttttgtttaa

```
14581  aagaataaga aaactatttg tacaagcaca aaaaagtctg gaaagataag taactgtggc
14641  tggtcatctt tgagctctga attagaggca agaaaaagaag ggaattaatt catgtgcttc
14701  tatcttattt gagtttgtta caaagaacac aggtgattct acaatcgtta aaaagcctcg
14761  ttaaaaacaa ccgtgttctg ggtatgagaa atcacgagtc atttacaagg tatgatttct
14821  taaaaacata actgatttag aaaacacatt atataccaga actcagtacc ctgggagatg
14881  tgatataggg acaatctcct tactaaccat gtacaactgc cactgttagc tttgtatgtt
14941  ttctactata gaactgcgta aacttggcca ggcgcggtgg ctcacgcctg taatcccagc
15001  actctgggag gctgaggtgg gcgatcacg aggtcaggag ttcgagatca gcctggccaa
15061  cacagtgaaa ccccatctct actaaaaata caaaaattag ctgagcatgg tggcacgtgc
15121  ctctattccc aactacttgg gaggctgagg caggagaatc gcttgaaccc aggaggcgga
15181  ggttgtggtg agccgagatc atgccactgc actccagcct gggcaacaga gcgagacttg
15241  gtctcaaaaa agaaaaaagg attgtgtaaa ctgaattctc tggtggagaa ggcaccatct
15301  gaggtcacct aagaaactgg gaagtatttt tgctggaagc aagcttggga caagacatga
15361  gatcacagca ggcaatccac taacctcaat atacaaaaaa agaaagagat gtaaggtgta
15421  aaggcagaaa aatgattgta tctctcatga ggatgacagg ctccaagtaa actgaggccc
15481  aaaagcttta cccaaggatg gaaccaatct cagaaaacca cacacaacaa atttaaaaaa
15541  ataaaccaaa gaaagggtgg gctatgtcca agaacacagc tttaaagacc ccctagaaga
15601  agcaagagag acactagtaa aatcagtata aaacagcaaa aatcaataaa taaaaacaaa
15661  aataaatgta gaatggcatg aatcttgatt acaaagtgct tttcctcatc aaagtaaaat
15721  ccaaaaagca caatcatttc aatgtaaaaa ataaaatcag acaagtctta aaagaaatac
15781  agctaagctt tggatgggag aagtttttct aacaaggcaa gaaactgaat gtcataaaga
15841  aatgattgac agattagact gtatgaaaca cagcaatttc tgtgtagcaa aaggcaccac
15901  ccaaaagaga caaataacac tcttgggagt atctataata tccacagact ttgacacagt
15961  cgaatgtagt tcttgaaaat cagtaagaag aaaactaacc tgcaaataag gaaatgggca
16021  acagttaata tatgaatcag tctccaaaga ggaaatttat aaagtcaata aacatatgaa
16081  aacatgccca agaatatata taaatgaaaa taataaactg ttcaataggc aaaaagatgt
16141  ttcaaaatgt gttaattcta atactgggaa ggttatataa aatcgggtac tcagggtact
16201  ggcgtatcct tcagaaagag tatactcaac aaaatacaaa aaaaaattta tctgacccaa
16261  tacttcaact actcgaagtt tattctagca agacaagcat aattggggaa gtacacaaaa
16321  atgtatgtac aaggatgttc atcatagtgt ttaYattaag aaaacagaga gccaaaatgc
16381  cctttagagg actggttagg taaatgatgc tatgtattac agcagcaaaa acagaagaca
16441  aaaaaatttt ttgttaatta aatacaaaaa tcattatgca tcattgctag atctccttga
16501  taatacataa tgtatagtta cagaaaaaca gatacccaag tcctacttac ataaaactRc
16561  atgagtgtat gtataaacat gtactgattg ttttcactac agaaaaacta aagccacttt
16621  taatttggga gaaaaatttt taaaaggcat gagagcagct aagagattaa agacagagag
16681  gttagtgcag acagcggttg acaccaggg aaagagctgt ggacctgct ggcctgaagg
16741  tttcaatatg gagcactgct ctccaggtcc ctgcatccac caacacagaa gacagtaaag
16801  gaagtctcct gagacattag cagaggctct ggacttaggg gaccaggctc tagagtggca
16861  aagggtagga gcaaaacaca tgaaatggaa agttgatgta aacaaacac agaccttcag
16921  cccccttcct cctcYgaggc ctaaaaagct gccaaccggg cttctcttcc tgtagtccca
16981  cctcacctca ggaaaaaaga ttaaagaaat tcttcatctg aagaaaatgc tgcttactta
17041  agcacccagt taacggctgt cagttgacaa gccatgtcaa caaggacttt cataatcaaa
17101  ttttggtaca agactcttca atgtgaatgg acagcaaaaa aaaaaaaaaa aaaaaaaaaa
17161  tcagagattt gaaggaagcc tctaacatag aagacagagg ccaaaaatga acacataaca
17221  tgaaaaaaaa aacattctga tgaaatacag aaaactgcaa agaaagtaaa cagtatttt
17281  tttaaaaaga caaaaaataa gtacaagctc ttggaaatta atgacaccag aaataaaagc
17341  aatcagtaaa ggatgaaaag ctaaaattaa ggaaatcttc ataaagtaga acaaaaaaga
17401  cagacatgga taacagggg agtcaaaaat aaagtaccgg gtcataatcc aggtggttgt
17461  ggagaaggtg cagaggggta ggggaggagg agaggaaaga aggtggagaa agaggataaa
17521  acaaataaga aactctaggc aaggaacatc actatacaat ttcagaacac cagggtaaag
17581  aaaagatcct aaaagcaaag tctcaaaaag gtcccRtttt gttttttta gaaatctttt
17641  aggaggtaag cctctaaaat aaggaaataa atcaagaaag aggatgtggg ggaatctcag
17701  ggaatctcag gatggcagtg gtccatcctg gagcaaRggg aaaagggatc cacctagtat
17761  gtgaggtctg acaaccagat gaattgtact cagagaatgt acaaggaact gacaaaaagt
17821  ttaaagaaat ctgagccaat tagagatagt taacttaaga aaaaaataaa aacgagttac
17881  acaagaaaga aaatattaat gcatgctact tggcgcaaca aagatcaata tctatctggt
17941  cataataaaa acattaaagg tctatgttac caaaagtgta atgtgttaaa ggaggatgct
18001  aatgaggaag aggacacaaa agagctaaga accatcatct accagaacaa aacaccaaaa
18061  gatatctcaa aagagtgcag tacaaatacg gagttttgga aaatggaggt aagtaccagg
18121  aaatacaggt aaaagagctg aaaactgtct tagggcaatg gaaaaaaaag atgaggagct
18181  gctttattat tcacacaaat tcctctataa aataaaaatt agtttaagga acacttaaaa
18241  gccaaccaga cagacaagct tagaaagaca gttctagaga cacctgaggt tgtcaccaaa
18301  actagcaaca ctgttacatg Raaatcaaag aacagggctc tgaagtgaaa caaaagccaa
18361  acctgaatct taggtctgct gcttagtagg tatcagcttt cccagattag actctctaac
```

```
18421  tctcggaaaa actcaaagga tgctgtctgg ccYgctgaaa ttcaatggca gctcagctat
18481  ttttaatgtt gctaaaatct gaatctatta atctgacatt aaagccaggc ataatgtaag
18541  tcaaaaaaga caccagaagc atccagcttg ctaagttagg caaattaatt tgtagctagg
18601  ctctaattac ccatgttaaa ggtaattcat ttctattttk actatttcta cactttacct
18661  tttctcttgg ttttcaagta aggttgaaag ccttaaaaag aaattgtgtc aacctaattt
18721  gtctacgcct aaaccatggc aggtaaaatg atcagaatgt tcccccaggc tgtgtatggg
18781  ggcggatgtt aagagtcaga gatagcgcac Rcaaagaaaa cgctcatgga acagaaagcg
18841  ataggagtca acaaccgaga ggcagggcgc tgaaatgaag ctgaccctt tcctcttaga
18901  attttcctc acaggattta gggtccccag tccccttgct ttctttctgt gtccaactga
18961  gatgttctgt gatgtggcca gccgcatgta ttcccctgga ggctctgacc caagccaagg
19021  cctgccttga acattcccag gcgctgacaa tgttgtttag gctattgctt gaaacactga
19081  gaaattaccc ctgttgctaa acacacagaa actatccctg gccctgaacc aaattcctcc
19141  aacactcaaa tcaactccct caccttggac acatcttttc ctgctgtctg ctgagaggac
19201  tgctgcagca ctaaatgctt ttgactgatt acctgagat ttagtgttct ggaaccccaa
19261  ctaggttcgg ggcagtccct tacaggaatt cctctgccc tactttagg gcaacttcag
19321  ccacaggttc agccagaagg aacacagaag atgggcttac tccaatgata tcctcatcta
19381  gacacttctg taacttctta tctcaatgga ctactrctaa tgacacagat ggactactta
19441  tccatctgtg tcaatggact actctaagtg acaaagatct gtcctgggac actgtacttg
19501  tatttgattt ttagatgcaa ccaaaagcca atccaaatga gaacatttgg attgcaaatg
19561  agaacaaatg gattggaaca tttggatgga aaacattggt gcccatgtgg cgtaatgcag
19621  ctctggaaca aaaatgggat ggaatattaa gtaacaagac ttaatattct cagggaatcc
19681  tggtctgact ctgacaaaat cagagaggtg tttcaaaaag ttctgaaaac actggagtag
19741  atgcttatta ttaattaccc caaatgactt ctagaaccgt ttaagaactt ttttgaagtg
19801  tatttgttaa taaaaaaatt ttcaatactc agaatcacat ttaggtcaag ctttctaggt
19861  ccggattttt tctataagat aaaaatgcct aattatttac tactaactca tgcaagttcc
19921  tgagaaaata gcaaaatcaac tggctgctca acattcacta ttagagcttc aatgtgcctt
19981  tggaggtcat acattagctt cagtttcttc atcacttttcR ttatcagaaa tgaaatgaga
20041  attgtgtcag atggtattta tggttctttt caactctaga tggatacaca catctaggga
20101  ataataactc ctccccccca ccattttcca gaaagaagga attctacctt cttcatcaag
20161  tccaccgatg atgttgtaaa catagtatgg aaagaagcgc cttgaataca ggattgtaga
20221  cagcattgca gcaattgccc ccgtagtcat ggccttatta ttggaatgct tatacatctg
20281  caattattga taaaagtcac aggcatgtag aggcagaggc cattatagac tagaacaatc
20341  aacagtataa agtgaataaa taaatgcata ccacagtgga aggggaaagc atgcctattt
20401  ccttcatgat caaccaacac agtattacta acataaaatt ttaagggaag gaatgccaag
20461  tttgccctca gctctctggt ttagactcta ttttccatac caccctttatc tcaggtactg
20521  ctaatccaag agctaatgtg tatgaaaggg cacatgaagt ggcctaagga agatgggtct
20581  aaatccatct ctctccctca ctctgcatat agaccagggg tcaacaaact acccctgtag
20641  tttggctcag gggccaaatc cagcctactc cctattgcta tgaatattgt ccgtggctgc
20701  tttttcacta cagaagcaga tcaaatgagg cccatcaaagc tgtaaatatt tactatctgg
20761  tcctttacag aaaaattacg gcaatccctg atcaaaccta gatgtaagtc cctctctttg
20821  tggagcagat ctctgtgaga acagaagaca cagggcagca cccttactct gcatgatttt
20881  aatacacagc agtggtcgtg atccttaaaa catctacagt agagaacaca agcatccaaa
20941  acagggttct agcatgacaa tacagtgact gcaaatccta gctttactat accttgcga
21001  gccctacatt acccactggt agagaaactt cacaaaaatt ataaacataa aatgaattca
21061  agatcaccaa tttttgttaa ccacatagca aacatctcta atgagaaact taatggccag
21121  gcatagtggc tcacacctgt aatcccaact gaggcgggag aatgtttgag cccaggagat
21181  gaaggctaca gtgagctaca atggcgccac tgtactccag cctgtgcaac aaagtgagac
21241  gctgtctcta aataatagta cagatagata tctaactagc accgtaaaat taaatatgga
21301  cagtcaaaac actgaaaaat gattagaaat gaactacaag taacaggtaa gttttttata
21361  gaggaatgcc tttccaagat aaaaactata aaaaattatt cataggccgg gcacagtggc
21421  tcactgctgg cctgtaatcc cagcactttg ggaggccgag atgggtggat cacctgaagt
21481  caggggttcg agaccagcct ggccaacatg gtgaaacccc gtctctacta aaatacaaaa
21541  attagacagg ggtggtgaca ggtgcctgta atctcagcta ctcgggaggc tgtggcagga
21601  taatcacttg aacccaggag gcagaggttg cagtgagcca agatcatgcc attgcactcc
21661  aScctgggca acaagagtga aactctgtct caaaaaaaaa aaaaaaaatt tcattccatt
21721  tcatttcgaa accaagcacc aacatttatt tacttcacca cctaataaag tatgagagaa
21781  aaacttcagg aaggggtgtg tattatgtag aattcaccat tccttgtttt attaacaata
21841  tcatgtttac ttttgtcttc taactcccat ttataaaata agcattagga attatcatat
21901  aaatatgcca ataaatgtaa gtcactatgg ctttcaatgt aagttttcta aaaagcatta
21961  acaattgata aatactgagt gaaatccttt ctacacattc aaaaagcatg tgtcagttaa
22021  ataaatatac tatatactcc agtaaccact cataagtgta aataatctca agtgttattc
22081  atgaataggc aaaacagaat gtgatcaccc ctgacttctg gcagctggct atcaactgaa
22141  gctggtcagg tgacagacgt taatggtgca tgttgtgcct cccatccaag ctcccagctt
22201  attcattctt tcgtatttct actcatgcat cctgccaact aagagcacag cactgtaaag
```

22161 aggaaaagct tgtcaactga tggtgatgca aaccaagctc ctgtgtcaaa tctttcctgg
22321 gctctctcct gccacagaaa ttgatttgct ttgtttttga gggaagagta tcttcagaag
22381 aagaactcct cccaggctcc ttctaaaagg gtagagaacc cttcatatga tacaagacct
22441 taacaaatgg aatgtgctgc tgtttcacat tatgctactt taatgaccct gcattaatga
22501 tatcatttca tttctagcat acatttgtaa ttcatctact aacctagtga ctctctagct
22561 atctgaccaa cagtcatgct gtaggcttaa aagaatttaa tgaatttcta ttaatttaaa
22621 atagtgtaga aatgtacaaa agcatctacc tttagtcttg cttcaataat ctttgtcagc
22681 gtaagacagt ctccatgaaa accgctgcat ccatgactg tttgtgtctt tctgtaaaaa
22741 gcacatttca gaaaactgag ctggttagat agtagagcaa aacatatctt cggcaatttt
22801 aaatttaaaa ttctgattcc cactattccc taaatggtaa tgggacaaac agtcaccctt
22861 ctggggagga ggggtctgta ttccatctta ccccttattc cagatgaatt acaggtggat
22921 caaagacttt aaaaatgcga ctatgaatgg actaaataaa tcatgggtga attttttta
22981 ctatcttggg ctgaggaaga tacgtaggta ggttaattga ctgatttttg agacggagtt
23041 tcgctcttgt caccccaggt ggaatgcagt ggcgcaatct tggctcactg caacttccgc
23101 ctcctgggtt caagcaattc cctcgcctca gcctcccaag tatctgggat tacaggcacc
23161 cgccaccaca cccagctgat ttttgtattt ttagtaSaga tgggggtttca ccatgttggc
23221 caggctggtc tcaaactcct gacctcaggt aatccacctg ccttggcctc caaagtgctg
23281 ggattacagg tgtgaaccac tgcaccccagc ctcgtgaagg tagatttaaa caacacaatc
23341 caaggccac acagaaaaat ttcataaatt tgactacata aaattctaca gggaaattta
23401 agaatagctt tttaaaaccc taagaaaata tattagtagc atctaMcccc aaagtctaat
23461 tttaattcta taaaaattct tacaaataag gaaagcaata acataaagga aagatgggta
23521 acttctatga acagacaagt cacagaaaaa agagacatta agtcaccata aacataagag
23581 cctctatgtt actcagaaat ccaaatctca aaaagagact atttcaacca attatactgg
23641 ctaaaaatgc ctaactaact aaatgctggt gaggttgtgg aaacagtata aactgattaa
23701 cctgttagat gggcaatttg gtggtatta ttaaaatttt aaatacacac cactctcacc
23761 aattctattg ctagaaatcc atcttgttaa tatacttatc caagtatgca aagggatgct
23821 ctagactcac cagtgagtac tcatttaaat agcaccccaa aacaaaacaa aacctaaatg
23881 tccatctgta tggagaggat taaaatttgg tatagacata caaattcaac cgtgtatttc
23941 aaaaattaat tcctagatct tgatatgaat ctataaagaa acctaaacaa tattttgcag
24001 aggccacaca attcctcttg gaaacttacg aatgactcgc acaaaccata cctgtcctac
24061 taggagagca gctgacacct ctagggtcat cactaacatc acctgatcta tgcctaccat
24121 caacctcact gcactaaggt gaagacgtcc aatcccctat aaggctttac tgcctttact
24181 gacaagattg gttgacaata ccaacaggga aagacagaaa tcttagaact tcaagatgct
24241 tttcccaaat atccaggtgc atcaaaggaa tgggagtttt catgcaaaga atacagtctg
24301 aaacaggttt ggaagaggca agcttagttc taggtcagMc ccacaggacg tgggatgagg
24361 gatatatata ggcattcgtt aatgctgcat tgttcttatt ctctatctct atatctgacg
24421 tgtttcacaa aaaaaaaaaa aaaaagtgct cacttcacca gcaaacgtaa ctaaagcaat
24481 atttaaaaga tgagtaaaag ctagtacaag gatggtatcc ataaagttgt tttaaaatct
24541 tattttctat atttactact ttcaagttgt acaagtgtcg tccttgagga gaaaaaaagg
24601 taacacaaga gcaccataaa cagaaagcag aaaggggga tcaaaagatg caagtggaga
24661 gaaacagaac tgggaagacg aaaacaaact tcattgcttt ttaagatgtg ggccatccct
24721 aggagcagga aagacaacgt atcttttctt ctgtacctac ttcctacaat acaaggaggg
24781 tccatccaaa ggacctaaac ctcgtaagtc ccattcctat tacaattcaa gtttaattaa
24841 cccaggaatt catgaccatt tataagcatt tccaaaactg gtaaatacag accactgcca
24901 atctgcagta tgtattcagt atttatgcag gcttttgtt tcttttaagtt ttggctttat
24961 tttcatgttt taggaaaaac atagctagcc tattaaaact gagctgtgga cataattgct
25021 taggatattt ctaaaacgaa tgtttcaggt aaaaaaaaaa agtgtgggga ggcagattta
25081 aaaaaaatat catttaatgg attaatggtg ctgtggttg aatattcct tcaaaactca
25141 tgttgaaatt taattgccat tgtgatggta ctgggagttg ggaccaggtg tttaggtcct
25201 agggctcagc tttcatgaat ggacattatc acagcagtgg gttgcttgc tcttctttct
25261 ttctctggcc ttccaccatg ttaagacaca gcaggaaatt tttcatggta aaatgctggg
25321 gtgaacacat ttaggttacc gaaagcactt ttggtaccct gaatacagca aatattatta
25381 agactgcaca ttaaattatt aggaaacatt aacttagaaa atggttttct aataaaaatg
25441 ctcccaacag caacttaaaa actcatgaaa caaatcattt agaagtagaa actctcacaa
25501 catYaaatca ttacaaaggc attgtgaaat gtctttagaa atatttactt acaatttgta
25561 acatttgggg ctatcccgcg tatgaattga aaacccttca ctcaatcgag tatcagaagc
25621 aacaattgca aaatcttctc cagcaattgc cagtatagta ctgaggaaaa aagaaaaaaa
25681 ttaattctcc agggtggtaa tcctatccct acaaatagaa gaatgctcca tagtacataa
25741 tgggataaaa tacttctagat gtcaacaaaa acatgattca aatgggaaga ggaaagatga
25801 gcgggaagag aatgaacgcc tggctacgag ttgtctgggа aaaaaaaatt attaataagc
25861 ctaaatcagg gcaaagtctc cttggcagga gttaacagaa aagccaatga attatcatca
25921 ccaacacatt aaatacttac tcgcgcaagg tactactaat acagaacaac taaataccac
25981 atctgtgccc ttgaggatca ggtatagaca gtggtactac aacgcaagct ctatgagttt
26041 agagaagatg agatttttttt ttcttgcttc atttctttat atccaagtcc ttatataacg

```
26101   cctatataat gcttatttct ttatacccaa tcccttatat aatgacaaat agatggacaa
26161   acagtaaatt tttccctctg tggctgtaca atttgacagc ttatcaaaga gacttacagt
26221   agaattccaa aagcagaccg cctgggttct aattctggct ttcccgtttc gcagatatga
26281   gactgtgggt aagttacttc tcaaagcgtc aatttcatca tatatacaac agagatcact
26341   gcagttgcta cctcattagg gtgttcaaag gatcaaatat gtaagccctt atagcaqtcc
26401   ctgacatgta actggtcctc tagtaagtgt tagctataag tgctatggca ctggagtatg
26461   actaagcacc tgggctctgg aattacatga gacagagacc cactcttgct acttactagg
26521   tatgtgatct tggacaaatc ctccaaatgc aagttgatga taacagtacc tgtgtcacaa
26581   ggtgtgtata tatatttggg tgtgtatatt ttaatgtaca agqcttgact gataactata
26641   accactgctt caatgcaata gtggaaatta aaggcatggt gcctcacaga cgtaagcact
26701   caqgaaactt aagccactat ttttactgag gagggatttg tgctaaagct ctcaagaaga
26761   aaaggatggc attccaggta atataaacag caagcaatgg caaacaggta attattcaaa
26821   taqtacatac attcaagcaa ctcattcagg cagccctttt tgcataagca catgtagtga
26881   cgttaaggtt tatgtgatgg acaggqttcc tactgtagaa aatcccaaat gccaagctaa
26941   agatttggga atttagcaaa gaaatcatga aggtattctg agcaagaatg atctgtagtt
27001   gtaactactc aagaggctqa ggtgggaqqa ctgcttqagc ccaggtgttc aaggctgcag
27061   tgagctatga tcgtgcctgg gcattagagt gagacctggt ctttaaaaaa ggaatgcaag
27121   agaqagaaaa gttccattta caaagtggqg ttttaggaag actgctctga caaYaacata
27181   gtatgtgaaa tgggacagaa acactgttct aatactacta atgcaatagt aaggtagcag
27241   ggtgaacaqt aaatccaaaa tcatcacaaa cacacaaaat agacaaattt ttatatctac
27301   gcaaatgttt taggaactgg gaaaaccaat tatgacatcc aagatttaga aagatttaga
27361   acagaatgat ggcataatta taagtatttt aaaggagagg aggccgggca cggtggctca
27421   cacctgtaat cccaacactt tgggaggctg aggggqgggg qqqqqgtcaa ttgcctgaga
27481   tcaggagttc gagaccagcc tggccaacat ggtgaaaccc atctctacta aaaatacaaa
27541   aattagccag gcgtggtggc aggcacctgt aatcccagct actcgggaqg ctgaggcaga
27601   aatgcgtgaa cccaggagtt ggagggttgca gtgagctgag atcgcaccgc tgcactccag
27661   cctgggtgac aqagtgagac tctgtctcaa aaaataagaa gaaaggagaa gaggagatga
27721   aggggaataa ttagcttgct ttttgttttg ctagctgtct tgagttgccc tgagagcaga
27781   aaaaccagtt aaaaatgttt tactgaagaa gccgaatcga gggactcatg aqaggcagaa
27841   ctggaaaacc agatttggga gtaatcctcc cagcaatgag acatgaaaga gtgctgagcg
27901   ataaacaagq cggctaatga cttaactaca tttaaagaca gagtaggaaa agagaatgag
27961   gcctcatttt gcggaagcga aggctgcctg agagccagct gcagtaaWca ctaaagaaaa
28021   agaacaatga ctgagaaaaa gtaatcagaa agatctaagt aatttttagg qcagtaatgg
28081   cttaaactgg attacaaggg attaaaaagt gagtaacgag tagggcatac tgaacactga
28141   aaattcttat ttatagagaa tagccttacg aaacgggtcc aataaccctc cctacaatat
28201   acaacttaat tagtcatcac agqaagtgtt aaggtgtata atqgaaaagc atccataaac
28261   tcagtggtga aatagctatg aattaagtcc tggctcaact tcacaccagc tctctgaccc
28321   tgacagttta acgtctaata taaccctagg atgctaatat catctaacat tcacttttca
28381   tgaggattaa ataagatgac agcttgcaat ttacaaaatg catcttctgt gattctcacc
28441   aaaaactatg aagctactaa ggaagataag gaaatttagg ttcaagaagt tcagaagtac
28501   ccaaagtgtc ctttagtggc agaaccaagg ctaaaatcag actttcgtta tctttctaac
28561   acactcccaa aatgtgcatt tatatttcaa atttatgagg aaccaattaa catttttgct
28621   ttgtttttaa aatttatttt tgtagagatg gggtcttgct atgctgcgca ggctggtctt
28681   caactcctgg cctcaagcga tgatcctcct gccttggctt cccaaagtcc tgggattaca
28741   ggtgcgagcc acactgccca gccaatattt tctgttttaa gaaccatcgg ttcgttcaaa
28801   ttgcgtgtgt atattttaat gtacaaggct tgattggtaa ctataaccac tgtttcaatt
28861   tacagctctt ccctgtcaag agtcttaaac agaqcatctt tctataaccc taaatctctg
28921   gcgtgccacc acggaaaatt atactactca agataaagct ggtaattaaa atcaaaacca
28981   aaacttgaac atacatacca agaacacaca tactaaaagg tccatcttct gagtattttg
29041   ttttcctgaa cttaagctaa acgttaaaaa aaaaaagcac ttatctatga aactaagttt
29101   gctcagccaa tcccaccttc tatttgaaat aaaacaaaat gattaaactg ctacaattag
29161   aaataacaga aatcaggcgg ctacaattag acatctcggc tacccaaccca gctatgcatc
29221   taacaacaca gaccaaacaa ccctaacttt taagtttcag acgctaaccc tctaccctcg
29281   ccggctggca taaRaaacgt gtacatgagg tccagtttta atggtcttcc acagagcaga
29341   ggctatgttt caatttctac tttactgtct tacagcagca aggagcacgg agtggcggtc
29401   cacataaaaa ctcaaatgac atgactgtaa tgggaaacca taaaaaccaa ggctgtatcg
29461   caatcaccaa gtaaacttga gcaaagcgag cctgaagagg gaaacacagg gcatgagagg
29521   acggcaqgga gaccggcctt gtgcggaccc cctcagctca gggttctgag gcctgcagga
29581   gcccgggaca gcgccatcac ggcggtgact cctaaatagg cttcagcaga tggggaaagg
29641   gcgaaagtga aagccgcagc tctctgggqt ttttaccctc cgttgaaaac gtagggcgaa
29701   aatcgcagct gcaaagggcc cgcggctctg tgcggttcca tccccaagtc tctgccagSa
29761   gccqaataca tggctqtaqa ggacaacatc gcacggctgc gcctgcggat ccgacacttg
29821   ctgtctcacg gcgagatggc tgccttgacc ggacgttacg ccacttccgg cttctcctga
29881   agttcgctcc cggcctctct atctcacgct agtcgttgct cctggagggc tgcacggcgg
```

```
29941  cttgtccctt tggtagttga atcccgccca ttccaaaaag cgctgacagg gatgtaaagg
30001  gttttttttg tttgttttct gtttttttcc ccctcgaaga aaacattgga attcacccca
30061  atggacaaaa atttaagtct gaccatacaa aaaaattgtc agaactatgg cgcaacggca
30121  actcgaataa cggtgggaac gttaattgtc ctggctaata aaaaatgtat ataacatttc
30181  ctatccttaa agagctcaca acctcactga taataaaaag tacaaagaaa acaagcagta
30241  taacatatga ttacgccaca atgaactaca gaagggaaaa tcaaggcgtg ctgaagtccc
30301  actaagaaac aactgcggaa agagccatgt gacaacagtg catgaactgg gagtggcaga
30361  actgaatata aatgcatgtg taaacacaag ctgtttgttt tgcttagtgt tccttgtcat
30421  tctacacgct tgaagatcag ctagcgttct tgctgacagg taaggaggac gcgcttactg
30481  agtgccaagc actgctcagg cactgattct gtcaatctct gtcaatctcc cgcagcccca
30541  agggtaagca ctgttatcat tattcaattt tacagaaaaa aaatgcgggg gagaggtcag
30601  gtcacttgtc gaaggtaacg ccgctagttg ctttaaacaa cacaacaaac aacaacaaaa
30661  cacactcaca catatacaca cacacgccat ttaaaaatcg atctttccta cgtccagcaa
30721  gggccaatta gagatggctg tggcacggcg gcccgcgccc ggaactcctc aagagcttcg
30781  ccccttcctta cctatggaaa cacaggaagt gacctatgct cacacttctc aYggcctccgg
30841  ccctagtggg agcaactcgc tgaagccgag ggcagaactg gcggaagtga cattatcaac
30901  gcgcgccagg ggttcagtga ggtcgggcag gttcgctgtg gcgggcgcct gggccgccgg
30961  ctgtttaact tcgcttccgc tggcccatag tgatctttgc agtgacccag gtaacagatt
31021  gtactctttt ctgacggttc gggcgaaggc caccactgca ctgaggcctg ggggcaatgg
31081  tggggaagag actaggaatt ggcgcgcgtg caggcccctc gggggacgtt cctccctttc
31141  gtgctgccgc cgttccggcc tgtaacggcc actccgccgc cactcccgcc tggtgcccta
31201  ctctgctgtg tttcgcaggc agcttcccat cgtacgattg tggggctcag ggtactactg
31261  gctggctggg cggcggcagg cgggacagga cagtccctg catcgaagac cctaagttta
31321  ccctgcccctg tcctgccatc cgcttcttct ccatgttaga agcagattca cccagatctg
31381  tgcccgcctg ttttgctgcc aacattgaga cttaaatatt ttgtcagaag cctgagacag
31441  cgggcacggt agcgcttaag atataatacca caccacttta tttgcagggt ctcccgtctc
31501  tcggttcagg ccatcatggt tttccaaatc tctaggtaga cttttctgtg aaaagactgt
31561  gcttcattta gttatacaga cactagaagg ctatgcagaa ttaatttgat tgcctccaaa
31621  aaatatcgga tttgatgttt caatttccag gagatgaaga tacccagcaa acaactcttt
31681  tctgaggata aattagtgca gtaatcactg tgcggtttct tctgtagact tactgcaaga
31741  aagtggcctg aagccaccga aggtcctgga taaatctcta atcatactta taatggcttt
31801  aaatcctgcc gtcattatct cttgcctcaa ccttagattc ctgaaacgaa acttccgtcc
31861  tccagtttta ctcctctcaa attcatctag tcttgccaaa ttagatctgt tcatactgca
31921  cttccgaaat tccataactg ttattattgc ctatgcaata acattgaaaa ctcctgatag
31981  tatgagccca ccaatatgtg ctgtctcatc tgctgcagtg accttctata cagtcatact
32041  aagctgttg cctgatactt gcatgcttt tcaatctgtc tctttctgct tgattctctt
32101  tttgtctgaa gccctgatgt gtaaattcct actcacctg tgagacccaa gttagatggt
32161  ccctgctttg tgaaaacact gcgctctctt cacagtgatt ggctgttagt ctatattgtc
32221  ttctcttcca ggggtgtata tgggctcatt catgatcaca tactgtattc caggcatagt
32281  gctagatgca gagatcacaa agacatgtag gctggtttct gcattcaagg aacttagctt
32341  agaccatacc tgctgttata atactatgtt ttacagtagt tatttgcata cccttcatat
32401  tgaacacttt gatgccaagg actatatcct cctatcttta tatcctcatc tgcaggactt
32461  ctgttattgt tattatagga taactgtcaa aaaaaaagta tattttaaaa aatatctctg
32521  atatatttat ttccagaagc agagcttgct ttctttttta gtctgttttt cagtgatgag
32581  tatgtaggat agatagtctt tgggggcctt tgccctttca aagtgatcgt cagagtcttt
32641  catacattca gcaaatatct gagtgtctgt tctgtaccag cacatgcttg aagtgcatat
32701  gcctgaagga tctttggaca tataattgt aacttgaga cctctaagtc ctatgtgaga
32761  atatgttgtt ataactcat ttcagatgtg tagtgagtaa agcgatgatg atttaagaaa
32821  agtcagataa caggcacagt ttgcattaat gtgttctaaa gaggtaaggt tattacattt
32881  ataaaaattc agggctttat ctttgtgcgg cttttttttt tttaacagtt tcattacagt
32941  aggagcttga taaatgatca ctctgaagta tattggattg aatttgatat ttacttaatt
33001  ttttgcccaa gacattgtag aggatgtaaa attggaatat ttaaagatct aaactttgcc
33061  taacagtgct gtgtatacag tgcttagtga atattctgct ctgatattac attttgctta
33121  ggaattattt ttctctaggt gtttttcctc aaaagttttt aatgctggtt atgacagctc
33181  gattttgagc attttccgat tatttaaaca tgtaacaaaa tgatttttgt tttgttggcg
33241  attttacatg caatcgccgg aaacatggaa ggaataaaac tttaggatta taaggtaaaa
33301  acaaatgtat tccaaaatag cttcattggt tttcatgttt gtgttttgta tagccataga
33361  actggcttat aggactgtac aggttacctg gatccttaaa ttaaacttta gacttttttc
33421  caaagcagca tcactgttcc ttggcgtgtg aagataaccc aaggaattga ggaagttgct
33481  gagaagagtg tgctggagat gctctaggaa aaaattgaat agtgagacga gttccagcgc
33541  aagggtttct ggtttgccaa gaagaaagtg aacatcatgg atcagaacaa cagcctgcca
33601  ccttacgctc agggcttggc ctcccctcag gtaatatagc aggagggaga gaatagggag
33661  ggcggaaatc tgaactgcaa gagatggtat caaaaggcaa ggaagggcat ttaatgatct
33721  gtttttgaaa atggtttaat atgttttttа agccttattt tgttgagaag ttctattagg
```

```
33781  ctttgaatag gcacaatggt gtttatttgg gaagtctgga agctaagtta tatatttatg
33841  aaacacctaa tcttttgata aacacttatg agaatgttcc aaatgactat ataggtcttt
33901  tgattttgaa aatcacactc accaaattat tttctagttt tatttttccc cttttacatt
33961  tcaagctctc aaccacccat ctacttttaa aatttttcag cctgggtgca gtggctcacg
34021  cctgtaatcc cagcactttg ggaggccaag gtgggcggat cacctgaggt caggagttcg
34081  agaccagcct ggccaacgtg gtgaaacctc atctctacaa aatatacaaa aattagccag
34141  gtgttgtggc gggtgcctgt aatcccagct actcgggagg ctgaggcaag gagaattgct
34201  tgaacccggg aggtggaggt tgcagtgagc agaggtcgtg ccactgcact ccagcctggg
34261  agacagagcg agactctgtc tcaaaaaaaa aaaaaaaaaa aaaaaaatca atacatttta
34321  ttgaaatata catacaaaaa aactcatttt aagtgtctgt tttgataatt atatataatg
34381  tataaattac agaacatttc agttacctta aaaagtccct tcttcccctt tatagtcact
34441  ctgctggccc caggtaacta ctgcatctgc ttttcaatgc tgaagattag ttttgtctat
34501  tctagaattt catatagatg gaatcagagt gtatgctttt ttgtgtatgt ctgacttctt
34561  agcccagtgt actgttttgta tatcagtagt taatccattg tatagctaag tatcactcca
34621  ttgtttggat gttccacagt tcatccattc tccagttgct cacatttggg gtctttccag
34681  tttggagcta ttgcgaataa aagcactgta aacatttgtg tagactttga atgcactgtt
34741  tttacttctc atgggtaaat acttaggagt aggattgcta ggtcctatat tggtatatgt
34801  atacctttat aagaaactgc caaactgttt tttgaagtgg ctgtattgtt ttgcagcata
34861  agagatttaa gttgctccac atcctcacca acactttctg ctgtcagtct ttttacttcc
34921  actctagtga ttgcttagta gtatcttatt gtggttttga tttttatttg cctgattact
34981  aatgtttctg agcaccttgg caagtgcttg tcagccactc atacacaggc ccacctcact
35041  ttactgcact tcactttact gcatgtttga caaattgaag gttgtggtaa acctgtacco
35101  agcaagtctg ttggcattat ttttccaaaa gtgtgtactc acttcatgtc ttgtggttag
35161  attttggtaa tttttgcagg atttcaaact ttttcattat tatccgttat tgttatcaaa
35221  cttttttttt tctttttttt tgtatttttt ttttaatttt ttttttcagt cactctgttg
35281  cccaggctgg agtgcagtgg tgcagtcttg gctcactgca aactccatct cccgtgttca
35341  agcgattctc ctgcctcagc ctcccaagta gctgggatta caggcatgcg ccaccacacc
35401  cagctaaatt ttgtattttt agtggagacg gagtttcacc atgctggtgt caaactactg
35461  gctgcaagtg atccatccgc cttggcctcc caaagtgttg ggattacagg catgagccac
35521  tgtgcctagt caaacctttt cattattatc tgttattgtg atcagtgatc tttgatgtta
35581  ctattgtaat tattattgaa tgccataaac tgcacctgta taatacagga acttaattga
35641  taaatgtctg cagcgtgacc aaccattccc ccatctctct ccctctgctt ggtcttccct
35701  attccttgag acacaacaat atggaaatta ggctaattaa taaccttaca gtgacttttа
35761  attaagtgtt cagatgaagg gaagagctgc acatctctca tttgaaacca aaagctatаа
35821  atgattatac ttagtgaaga aggcatgttg aaagctgaga caggctaaaa gctaggcctc
35881  ttgcaccaaa tagttagcca agttgtgaat gcaagggaaa agttctttaa gggaaattaga
35941  agtgctaatc cagtaaacgc acaagtgata agaaagcaaa acagccttat tgcttatatg
36001  gagaaagttt gaatggtctg gatagaagat cataccaccc acacatcccc ttaagccaaa
36061  gtgtaataca gagcaaggcc ttaactctct tcaatttctgt aaaggctgag agcggagagg
36121  aagctgtaga agaaagtttt gaaactagca gaggtttatt cagagcttta aggagagagg
36181  ccttctccac aacataaaaa tgcaacatga agcagcaagt tatctggaag atctagctga
36241  gataattgat gaaggtgact atactaaata atagattttt aatgtagatg aaacagcctt
36301  ctactggaag aagatgctat ctaggacttt tatagctaga gaggagaaat cagtgcctag
36361  cctcaaagct tcagaggact ggctgactag ttagggggcta atagagctgg tgagtttaaa
36421  ttgaagccaa tgctcatgtt ctgctctaaa accatagagc ctaagaatt acgctaaatc
36481  tactctgcct gtcctcagta aacagaacaa caaaacctga tgagagcacg tctgtttaca
36541  gcatgattta ctggatattt taagctcttt gagatctgct cagaaaaaaa gtttaatttc
36601  aaaatattac tcacgacag tgtaactagt tgtccacaag ctctgatgga gatagaacaag
36661  gagattaata ttgttttcat gcctgcttaa ataatatatc cattcttcag cccatggatc
36721  aaggagtaat ttcaactttc aattcttact atttaagaaa tacagcaggg catggtggct
36781  catgcttgta atctcagtac tttgggaggc caaggtggaa ggatcactca aagctaggag
36841  ctcaagacca acctgggtaa caaaacaagt ccctgttgct acaaaaaaaa attttttttt
36901  aattagctgg tcatggtggc atgtgcctgt agtcccagct acttgggagg ctgaggcggg
36961  agggtcactt gagtccagaa gttaaaggct acaatggaga ccctgtctca aagaaaggaa
37021  gcagggaggg acatatgctg tagctgccat agatagtgat tcctctgatg aatctgggca
37081  aagtgaattg aaaaccttct gaaaaagatt caccattcta gatgccatta agaatgttca
37141  tgattcatgg gaggagggtg aaatatcaac atgaataaga gtttggaaga ggttgattcc
37201  aaccctcgtg gatgactttg agaggttcta gacttcagtg ctggaagtta ctgcaggtgt
37261  agtggaaata gcaagtgaac tagaattaga agtgaacctg aagatgtgac tgaattgctg
37321  caatttttg ataaaacctg aacagatgag gagttgcttc ttgtgagtaa gcaaagaaag
37381  tggtttcttg agatagaatt gactcctggt gaagaactga tgacttataga atattacata
37441  aacttagttg ataaagcagc agcagggttt gagaggattg actccaattt tgaaataagt
37501  tctagtgtgg gtaaaatgct gtcaaatagt atcatatgct acagagacat cttcagtgaa
37561  aggaagagtc agtcagtgtg gcaaacttcg tcagtcttat tttaagaaat tgccacagct
```

```
37621   accaccctga tcagtcagca gccatcaaca tcgaggcaag atcctctgtc agcaaaaaga
37681   ttatgatttg ctgcaggctc acatgattgt tagcattttt agcaataaag catttttaaa
37741   ttaagttata tacatattat tagacataat gctattgcac acttaataga ctttagtgct
37801   aacataactt ttgtaggcac tgggaaacca aaaaattgat gccgcttgct ttattgagat
37861   ggtctggaac ctaacctgta gtatctccga ggtatgcctg tatcttcatt tgtaatatgt
37921   ccttcacatc ttttgccctt ttttattatt ttatttgttg atcttctttt atggagttgt
37981   cagagctctt tattattctg tttaccagtc ctttctcaga tgtatgtatt atagttattt
38041   ttttcccagt ctggcctgcc ttttaatttt ctcaatggtg tctttcaaag aacagaagtt
38101   tttaattttt ccgaagttca gtttatccat ttttcttcat gtttatccac tgtgtggtat
38161   taaagaagaa agcaatgtgt ataagaatag ctggttcttc cgtaattaat gtttaataac
38221   cccattattc tccgaaggca tctgtctttg cacacctgac ctgctgttcc accaagaaag
38281   ttccacaaac acttagcagc agccagccta acctgttttt ctccttgctt tccactagggt
38341   gccatgactc ccggaatccc tatctttagt ccaatgatgc cttatggcac tggactgacc
38401   ccacagccta ttcagaacac caatagtctg tctatttgg aagagcaaca aaggcagcag
38461   cagcaacaac aacagcagca gcagcagcag cagcagccaac agcaacagca gcagcagcag
38521   cagcagcagc agcagcagca gcagcagcag cagcagcagc agcaacaggc agtggcagct
38581   gcagccgttc agcagtcaac gtcccagcag gcaacacagg gaacctcagg ccaggcacca
38641   cagctcttcc actcacagac tctcacaact gcacccttgc cgggcaccac tccactgtat
38701   cctccccca tgactcccat gaccccatc actcctgcca cgccagcttc ggagagttct
38761   gggattgtac cgcagctgca gtgagtactt cgtgttttat gtttcctccc acttaggagt
38821   ccctttgagt tatgttcctg ctctgttttc agatggatcc ttttattaag ggagggagtg
38881   gcactaacgg taattgtgta tcaaaatttg ctttatctca catttgggaa agggaagcaa
38941   agctatctta gtcagtgtcc tcagtaaaag gctcttaaca ggtttagaaa tgtggtcatt
39001   tgtgtttaca tacctgagcc aataaaattt aatctgactt tcactgtcgt tattattata
39061   ttatagacat ttcctgtat ctgatatcgc taaatcacaa tgttaggtag tctctttccc
39121   ttatgctatt ttaggtcttt agtcacaata tcagtataat ttctggtagt tcttgttttt
39181   tgtttttact atgggtgctg catataaatc tttgaaggtc tgtgtccttc ccacaaaatg
39241   aagacgactg tttttgtcat aaatggattt ttctacctaa atgaagtggg ttctatatgt
39301   aacagtgtag taggggtagg aaataatttc atcttcctga aaaaccagca aatatttcca
39361   aataattcca gtcaataaga agtgtatagc ttttcatttt agaaagctta tgaccaaatt
39421   aaaaggttac ttgcagtctc tgcatctcct cagttttctt gtacagatac cttcctcctt
39481   catactccct ttagatctag tatttcctat ttgcatttat tcaccttgtt acatatatgg
39541   ttgttgttta taagctatct ctcatcattt ttggaactaa gtggtgtgta atcgtggatg
39601   ctgacttcca cccaaagacc taaatcttgc ctccacaatt ttgtttgacc ccacacacaa
39661   ttttaaaaac aaagtaattt tagtgatttt agagagagcc ctttttagct caccccttgtc
39721   tataccactc ccatgtgtcc agcatgcttg tctgactccc aggaatattt aagtttgcat
39781   ttctgatttta aataataaat tataaacagt acagtcaggt gttgttttct tgcgagtgcc
39841   tttgctgttc tgatactccc cagagcatcc agtcatccac atttcctgaat ttccactatc
39901   tactaagaac cctcccgggt ggtagttcag tgccctctcc atcttgtagg cttaagaggg
39961   attaaggtaa atatttaatt aatgaaaata tataagaata catttaacaa ttatgtgact
40021   aaagttgtga tagatatact aaaatctact tggtatagtt cataagtgga caaatgctaa
40081   aggcaggtgt gtatacaagg gtgattggaa ggaaatagat gatatggaaa tgaaaacatt
40141   cattgtgtgg atcaacctaa ttggctttac agttgtgtat catagactgt acaagaaaaa
40201   gaaccagaag caacaatgag ctgaaaccta ttgtatttga acctatgtat ttgaaatctg
40261   gactcgatat tcttgggatg gtgatttcca ggtccatgcg agacagttgt tgagcagtta
40321   attgcattca aagggcattg cccatttcaa ctatatatac tttcataagc agaaaaatgt
40381   ataatgaaaa tgtgggtttg ttgtttaaat ttttattaaa atttctaata gagttgcttt
40441   ttagtatatc tttatcctta tataagttat tcgttaagtg atttaagaac actgagaaat
40501   gaaaagggtc agtggacccca gatggctcca tttatcctta tttactgaga gttaattaga
40561   agagaaagca gggttttgcc ttttttttt gctaaagaca cttagctctt gttttcaaaa
40621   agatacttac tttgagagaa ctgggcagtt catgcctgct tgttttcatt ataaatagtt
40681   acttaggaat agggtggtgg tggtagcttt tcagagctca cagatgagaa ttgagtttgt
40741   ctgtgagaag gctaagggca ggctctggag acagacagac tcaaatcctg gctcctccac
40801   ttgggagcca ttgcgtcctg agcaagttgc actctacctt taagcctcag cttatttatc
40861   caaatgtggg aatactggta acttctacct cagtgcgtta tatgtattaa atggaataat
40921   ctatataaaa tgctcaacat gtgcatgata cttgttaaac aataaatgtg agcaattaaa
40981   aaaaagtaaa gcctggttga aataatcaga tgtctgcata atttctaacg cctcatccaa
41041   tgaaacttaa gtaatttaaa tagtcgtgtt ttcttttaa atctcttaca gaaatattgt
41101   atccacagtg aatcttggtt gtaaacttga cctaaagacc attgcacttc gtgcccgaaa
41161   cgccgaatat aatcccaagg ttagatctat tttaatgtat ttctttttt tttctttttt
41221   gtctcctctg ccgtgtctct atattttaat gtatttcacg ctataaaaca aatgtctgta
41281   gatcaggcca ggcacagtgg ctaatgcctg taatcccagc actttgggag gctgaggaag
41341   gagaatttct tgaacctagg agttcaccac cagcccaggc aacatggcaa gaccctgtct
41401   cttaaaaaaa aaaaaaaaat tggccgggct tggtggctca cacgtgtaat cccagcactt
```

```
41461  tgggaggccg aggtgggcgg atcatctgag gtcaggagtt caagaccatc ctggccaaca
41521  tagtgaaacc ccgtctctac taaaaataca aaaatttgcc gggagtggtg gcatgcgcct
41581  gtaatcccgg ctacttggga ggctgaggca ggagaatcac ttgatcctgg gaggcagagg
41641  ttgcagtgag cggagattgc gccattgcat tccagcctgg caacagagcg agactccgcc
41701  tcaaaaaaaa aatctgtata tcaaagagtt tgtgttatgc ttattccttg acaccaataa
41761  aatgaagatc taaagtaaaa tgtgcattgt tttgtatctt tattgagtg tctgtgatat
41821  aagaatccct gggagtacag cagtctataa aataagctaa gttatatatg tattgtattg
41881  ggatcatgtg aagaattttg tatatgtata gggatgatgt tagccagcta tagtaggcaa
41941  agtaatttgg ataaacatta gctgggttga gagaaatgtt aagtaatgga cttagggtgc
42001  attttaaaat ccctgaaaca taatgcctga gatctgaaag acagctaagg gtctgaaaat
42061  caccttttaa ccactcataa tgagtctgta tgacatgtag cattctaaga attaatcttt
42121  catctattat aatcacattt agttgaatac ataatttta tactttacgt tcttaagtga
42181  tatttaacca ataaaaatag tagaggaaat tctggaaatt caaaatagct aggcttttcc
42241  tgggacgtat ataaactact atatactgct agctttttta gatgttgata aaatcacagg
42301  gaagacatag agcaggtttt aaactaaaat tgttaaaagc caggcatggt gactcagacc
42361  tgtaattcca gcactttggg aggccaaggt gggaggatca cttgaggcca acagttcaag
42421  acgagcctgg gcaacatagc aaggccttgt ttcatcagaa aatttaaaaa atattctggg
42481  gttggtggca cacacctata atcccagcta cttgggaggc caagacagaa ggatctcttg
42541  agctcaggaa ttcgaggctg cagtgagcca tgattgcacc actgcactcc agtctgggca
42601  acaaagtgag actcttgtct ctaaaaaaaa aaattaataa aataaaaaaa taaaattgtt
42661  aaagcaatct agtttgtcaa agagtcgtct tattagaaaa catgtaggtt tttattgtat
42721  aattaaatgt attaaaatat ttaagttgtt tcaaagtaat tatttgcttt ttatcatgta
42781  cctaataact gaggccatta attcaacccа cagttgaaat atttcccct tgagttacca
42841  ccttagcaag aaaatttct gaaagaatta acatgtttca agcataaaaa gcagaaaata
42901  aaagtaaaa ctgtgttttt ttcctaattt gcatttatgt gtttaatаca ttaatattgt
42961  ttctaaagac caattgaaag catgatttta cttcattacg tattgatagg cttgtaatct
43021  gatttattaa ttccattaag gtagaaaagg tttattggtt tatttgcctc aaaattcata
43081  ttaataaaac aaaatgtatc agagaagcta tagtcatgat aagcagcaaa tataaagtag
43141  aaacagaagc acttgtattt attgagaaca taaccaaatt ttgcaaacat ttctcttgat
43201  ggaatgctca tgtgaaagaa catacagatt tggtataact tagtcacaat tgattatttt
43261  ctgctcctta tgcaaaggaa tatttgttac atgtggtgta tgcaaatcct ttacagatat
43321  acagaaatac agaacaaata ttttgataac tagatgtact atgtccttcc taccagttgt
43381  gatttttttg tcaatgggtg gttcgcctaa caacattgag cagtttggca tgacctcact
43441  aatgattctc tctgaccatt gtagcggttt gctgcggtaa tcatgaggat aagagagcca
43501  cgaaccacgg cactgatttt cagttctggg aaaatggtgt gcacaggagc caagaggtag
43561  ccgtaagaaa ttcattcttc tggttctatgg gttatgaatg aaaaggtgat atctcattgt
43621  ttttaggtta ttaggttagc actttaacat gttattattg cttttctata aaaaccattt
43681  taatatgatt ctattaatta tttttattta tttatttatt atttgattct attaatgtta
43741  gatagcagtg atttcatttt cttaaaaatt agatatgggc aggcgtggtg tctcaccaag
43801  gcgggcaaat cacttgaggc caggagttcg agaccagcct gaccaacatg gtgaaactcc
43861  atcttcacta aaaatacaaa aattagccag gcgtggtagt ggatgtctgt agtcccagct
43921  acttggagg ctgaagcacg agaatcgctt aaatccggga ggtggaggtt gcagtgagct
43981  gagatcatgc tactgtactc cagcatggga gacagaacaa gaccatttct ccagaaaaaa
44041  gaaaaaaatt aggtaagatg taatacaaca tcagaactat taataaaatt ccctttatgt
44101  gaaaaatgtt gtaaataaca caaatacatc ttgaaatgga agaaaaaatt gatcaagaat
44161  taaaacactt ctaagctaat ggtgtaaggg ctttgcagac cttattgggc ctggcagcgt
44221  gacagcatca catggtgttg ctgcagaaac ctgccttctc actggaacta gctttcatta
44281  atagtgtttg agttgtgcag atcttaagga atgcaccctt gttatаaaat gtcattgctt
44341  atattctcca tctgaagtga tcctgtctga aggttagtac tctgcggccc tgactgttct
44401  aaacagagct tatatacttg gtagaagtca aaaactaggg ggaaaattag tgacattagc
44461  ttcataaatg aactgaacaa ataaactaaa actttttaaa tgaaagagta tKaaatgtac
44521  ttggaggtat caacacatag aaggggctg tggatatttt tgcttattct gaagtttgaa
44581  attgtctttc agtgatggga atgccattgg tgtggacatt ctggctcctg atctccgagg
44641  tttttcagaa tgcaggacaa ggatgtgttc ttgccttca cttcccctg gccacaacat
44701  gcagtagtaa cctctttaat taagagcgtt tttgtttgct tgttttcccc tgcatggaac
44761  atcagaaact tttggtttat caaggcaagc ttttcatgca gcatttagcc tttttgtccc
44821  agagcatctg aaaactgaat attgtatatS tagttggatg actatttcat caagacaaga
44881  aacccaccaat acatttacct gaaatttaaa agcgtagcat atatatatat gcttgatttt
44941  tgttcttcct gatcccctgc acctgatagt ctctttatgg taatatttta acattctttt
45001  ttgttgttgt tgttgttttt gagatggagt ctcgctctgc gcccaggctg gagtgcagtg
45061  gcatgatctc ggctcactgc aagctccgcc tcctgggttc acgccattct cttgcctcag
45121  cctcccgagt agcagagact acaggtgccc accaccatgc ctggctaatt tttgtatttt
45181  tagtagagat ggggtttcac tgtgttagcc aggatggtct caatctcctg accatcgtat
45241  ccgcctgcct cagcctccca aagtgttggg attacaggtg tgagccaccg tgcccgaccт
```

```
45301  gcctgcctgc ctttttctct tttatttttt ctttttttct cttctttctt tctttccttt
45361  tcttttttt ttttttttt ttttttttg gtggagtcac ctaggctgga gtgcagtggc
45421  acaatcttgg ctcactgcaa cctccacctc ccaggttcaa gtgattctcc tgcctcagcc
45481  tcccaagtag ctgggattgc aggtgcctgg caccatgccc agctaatttt tgtatttta
45541  gtagagatag ggtttcacca tgttgaccaa gctggtctcg aactcttgac ctcaggtgag
45601  ctatccgcct tggcctccca aagtgcttgg gattagaggc gtgagccacc atgcctggcc
45661  cacattctgc ttttcttatg taagctctga actgctaagt cgtagtttat tcaacaaatg
45721  acataggaat gtctattcat gatgagtctt ggtataaaag agatagaat tagtgaatac
45781  attgttcaat aataaatctc atcaacattt tctgatcaaa atgaagtttg ttagttttcc
45841  tctcagtaga aatgcatggg ctaaaataca gaaatagtga tgaYtgatga tggtgataat
45901  tcacatccat aaaatctagg gctacaataa tttggcggat tgaaaggtca ttttggcagg
45961  cctacagttt tctgtcaagg atccaggaat actttataag gaattgtgaa tgcctgtcag
46021  tcttttctcc tattgcaaga aggctgacca gtttacactt tattagttta ctgttttgga
46081  cttttatata gttattagtc taaataagta ttttagctgg ctctgagtat gaataactca
46141  cttttttcct ttccctagtg aagaacagtc cagactggca gcaagaaaat atgctagagt
46201  tgtacagaag ttgggttttc cagctaagtt cttggacttc aagattcaga aRatggtggg
46261  gagctgtgat gtgaagtttc ctataaggtt agaaggcctt gtgctcaccc accaacaatt
46321  tagtaggtaa gtctgaaatg tattRtgatt gttattggca acagttcatt tataatctaa
46381  acattgttca gaataaaaca catgcaaaat attcagtata tgagaacagt tgactggttt
46441  atagttgtat gtattcttgc attgtcttcc tgatgttctc agtcatattt atcaccctca
46501  ccagcctctg cttcccttat cactttgcgg tacccataac tccccttttac tggaatgaat
46561  ttgattctac ttctgtatgt tttatcgttt tattgctgaa tacacttgga atgcatgaat
46621  tgaccctaac cttgtatcaa ttttttttcc cagtttggat cttctctttt agtcaacatt
46681  gtgtcagatc taccagcaaa gtgtgaagtt gagcgatagg aacaactttc taattatctt
46741  ccctgctact tgcaggtgaa gactcacagg caggcagccc tgcccacctc actgcttcat
46801  ctcatggttc tctggtgtct gttcacaggc acattagttc tgtgtgccca tggggctcac
46861  ttggttcctc ctgccctagg ccttgcact tgccactttt atgcctagta tgctcatttc
46921  ccttttcacc taggaagctc ccacttgagt tccatatgtc tacccattcc actcttcctc
46981  agagaagcct gtcctgaatt ttgtcttagg tcagacacac agaaacagag gcatcctgtt
47041  ttcagtctct ccgaactgag aaaaatgaga ttactaggct tagaagaata tgtaccaggc
47101  ctggcctggt ggctcacacc tgtaatccca gcattttggg aggccgaggc aggcagatca
47161  gttgagttca ggagttcaag accagcctgg ccaacatggt gaaacctcgt ctttactaaa
47221  aatacaaaaa ttagctggac atggtggtgc atgcctgtaa tcccagttac atgggaggct
47281  gaggcagaac aatcattcga acccaggaga tggaggttgc agtgagccaa gatcgtgcca
47341  ctgtactcca gcctgggcga cacagcaaga ctccgtctca aaaaaaaaaa gaatatatac
47401  caatagtcca ttcagtcaga cagcttaatc aggtatagat taattctcag gctagtatat
47461  aagttgatt aaatttcctg accacaattg tcagctagag aatattttca tttaaggagg
47521  taagatatga ttaaaagtta aactgtcagt attggatctt agaagtaaat gattattagg
47581  actgtaatag taattattag gactgtaaaa gtaaaggatt attatctgca ttagatatca
47641  ttatatctaa tgatatagag actgcagaca taactacagg gctcttttcc ttaaatcaga
47701  aaatccagat tcaatagaaa tagggtaaag tgataggaag acaaatagcc ttccatccag
47761  tggttatcaa ctgacgacta caagtcggcc tcacttgctt taattattct attctatcct
47821  ttgatgctgc ttgaagaact gtgttttacc tcttgactag tttgttttatt cagtatttttt
47881  ccttgtacag gtcctcattt tatctaaaag cacacaaagc tcttgatttc taaacttttt
47941  gcaattttcc ttctagttat gagccagagt tatttcctgg ttaatctcac agaatgatca
48001  aacccagaat tgttctcctt atttttgttt ctggaaaagt tgtattaaca ggtaagttgt
48061  aacagggaagt agtatctgaa agttgtaag tgttttgagt atggcatttt ctcagtgctg
48121  aaaaggaaatt tcagtgttcg gactgtggac tagcttcttg tacaaaggcc tcccaccaca
48181  agtctgatga gaaacgtgcc cactaaaggc acagtgagag cagggaagtc tgaccacagc
48241  tctgcaagca gacttccatt tacagtgagg aggtgagcat tgcattgaac aaaagatggc
48301  gttttcactt ggaattagtt atctgaagct ttaggattcc tcagcaatat gattatgaga
48361  caagaaagga agattcagaa atgagtctag ttgaaggcag caattcagag aagaagattc
48421  agttgttatc attgccgtcc tgcttggttt atggcctggt tcaggaccaa ggagagaagt
48481  gtgaatacat gcctcttgag ctatagaatg agacgctgga gtcactaaga tgatttttta
48541  aaagtattgt tttataaaca aaaataagat tgtgacaagg gattccacYa ttaatgtttt
48601  catgcctgtg ccttaatctg actgggtatg gtgagaattg tgcttgcagc ttttaaggtaa
48661  gaattttacc atcttaatat gttaagaagt gccatttcag tctctcatct ctactccaac
48721  ttgtcttctt aggtgctaaa gtcagagcag aaatttatga agcatttgaa aacatctacc
48781  ctattctaaa gggattcagg aagacgacgt aatggctctc atgtaccctt gcctccccca
48841  ccccctttct ttttttttct taaacaaatc agtttgtttt ggtcacctta aatggtggtg
48901  ttgtgagaag atggatgttg agttgcaggg tgtggcacca gattgatgccc ttctgtaagt
48961  gcccaccgcg ggatgccggg aaggggcatt atttgtgcac tgagaacacc gcgcagcgtg
49021  actgtgagtt gctcataccg tgctgctatc tgggcagcgc tgcccattta tttatatgta
49081  gattttaaac actgctgttg acaagttggt ttgagggaga aaactttaag tgttaaagcc
```

```
49141  acctctataa ttgattggac tttttaattt taatgttttt ccccatgaac cacagttttt
49201  atatttctac cagaaaagta aaaatctttt ttaaaagtgt tgttttctta atttataact
49261  cctaggggtt atttctgtgc cagacacatt ccacctctcc agtattgcag gacagaatat
49321  atgtgttaat gaaaatgaat ggctgtacat attttttact ttctttcagag tacttctgtac
49381  aataaatgca gtttataaaa gtgttagatt gttgttatac cttgtaagag tcatgtgatc
49441  atactgtttt ctacaaagtt gtattttaga tataatgcct gaaaccattt tggtgtttgc
49501  ttcagtcagt atttcattgt atgctgcaat gaaaacagat taatgatctg agaaccttcc
49561  atatattgag caactcctgt tttctaggta ttttgcatac aatgcctgga atcctcacaa
49621  agcttcagtt acgttttgtt cctctgttgg aggtgaggag ataaggaagc cccagctgag
49681  ggacttggct gaggttacac agctagtaag tggtaaaaat gagtgagtcc ttcaggtgta
49741  gaagctggtg ccctatccac aggctgccaa ctctctgcag taacttttttt ttgcttgttt
49801  tgcagttttt ttctcatgga ctatcaggtg gacatttgtg ggttcttagg ttttattgtt
49861  agagtggttt gttgttttta attgtaaaag tacatcttca gctgactcag gaataaaatc
49921  agaaaggggga ggtcctctct tcctttctct tctgcctctt tccccaagat aacgaccaga
49981  ttagtgggta tcttctaagc cctgttctgt ctatcttctg ggcatggcat ttgatcccat
50041  ttttggaaaa aagaaataat acattcaatt ttatagcttt ccctttttttc agtcaatata
50101  tcataaacct atttccatga ttgggaatct aggatactct tcttaggtac cttcacttac
50161  tgagctattc ctgtaattat ggtcatttac atgacctcta gtttttcaat atcatcaaca
50221  gcgctgcagg gaacatcctt gtatgtgtat ttttcggatg agtgcaggta ttcatgtagt
50281  aaacttttct agaagaggaa ctaaagacta tacattctga gttttaatca gttgatacca
50341  gattgcagtc caaagagaac ggtgcatgaa atgcccttt cttgcatttt ccaatcatta
50401  gtgatgccaa taatgtatgg attaattgga aagacatcat tccaatatta tctcctatct
50461  aagaaagaag tatctcttca tgtatgtagg ttctattgtc ctcagtaaag ttttgtactt
50521  tttttcacac agggctttta tatttcataa gtattacttc cttaattcct aagtatagta
50581  tcattttctgt tttattactg gaagttttc ctaacacttt aaaagttatt gttgataata
50641  ttttttcttat tccgagttta ctgacttcct attactgctg atttagttga ttgcattgaa
50701  agttctaggc atgtaatcat ctgtaaatag taattttatg ttttccttic caacatttat
50761  ttttcctatc agtgcctagg actttaatgt atataactta aaaaaaacat ctcttagagt
50821  tgtagctaca tatacaggaa atctaacaaa tgtgtagcat aatgtattat acaaaggcag
50881  acaccctgc agccaccaac aaggtcaaga aacaattttg ctgcctgtcc tagaagcccc
50941  tccttatggt cctatccaga cacacacttc tggcttccct caagcagtga ctattatcct
51001  gactctcacg catttaaaga taattgaagt tcctcgtcca tctcttttct ttccaattta
51061  caggccattt agtgtgtaga gcttctcata gtctggggtt tgctagttgg aaattcatgg
51121  tgtagtttcc ctattctctg tatttcctgc aaattggaag ctgctgtgta attcctagat
51181  ctattaattc attagtgggt tgcaaaatga catttagtc atttcatttc tttttcattt
51241  atataattga atacttttat aaagtgttgt gctccatata gcagaatact ttcccctttt
51301  aagttttcaa gataaaatga gttcatatta atatgtccaa ttcaaagctc atagggttat
51361  tttaccaatt gtatatccaa ttcaaattca aagcttatag ggtttttatt taaccaatttc
51421  tgtattacac tcttccttct acactgagaa tttttaattc ttaaagacat aggggatgag
51481  gaattagaat gtcccataat tactcattta ctttacgtat ttacttttatc attactttat
51541  ctgttatatg tgcaatttttt tttgagacac ggtctctgtt gccaggctg gagtgcagtg
51601  gcacaatcat ggtttgctgc agtctcaaac tcctgggctc aagtgatcca cctcagcctc
51661  tggagtagct agccaggact acgggtgcac accaacacac ccagctaatt ttttttaatt
51721  tttgtagaga caaagtcact caactgttgc ccaggctgtt cttgaactct taggctcaag
51781  ccatcctccc acctcacca taacattctt aagagtaaca aaaacactat caccaatatg
51841  attgccaaaa acacttggaa cttttttttt ttttgctgtg atatctgaaa ttgccaaagg
51901  atattcagta tctgaaataa aaaggcaaag ctgaatatgc tgcctctcac agcagaggga
51961  gctgctgtgg ctggacagta tctgcccaca gcagatctta aaacttgta ggtgttgaga
52021  aatggtggat gcatggactg gcaccgtctg tggagccatg attatgtagg tgagacttgc
52081  tcattatctt gtagtgtttt aaaatgtctt cacatttcta aaggcaactt gcttaatgca
52141  ttttttaatt taaatttttt atgttgtaca gtttatttta aatatagttg ctatttttta
52201  acacagatgc caagtcggtg ctgtgagatt ttctttctgg tgatttggac cagtttgtct
52261  ccctcttgat atatccatcc caaatggaaa ggccctgtaa actgttacga tcatctccag
52321  aggttaactg gaatatacac caatgacagc ttgcctgggt atgccaaaat acctgcaaga
52381  atgtccacat catctggtga tgtccccaaa taacagtttt taccatagaa agatcgttaa
52441  catgtttgct ttaaaagtca ttagcagtca taacgtactt acagattctg cctataagga
52501  ataatacata attttagata taaaggcccc actagtccag gtttccttat gccactgtgc
52561  ttcctactaa gtgttgcgac cagctctttgt cactagttga tgacaacttа ctccagtagc
52621  cacagggctg tgacacccata gttataggtg atttcatag atttagccat cccagggttcg
52681  aaactagtat cctctagctc ttaagtagct gataacctcc ccatggagga aactccatac
52741  tgcagtttcc catatggtgc tatgtataac tatcttatac aaattaataca aattgcatat
52801  gtatacttat ataatatgga ctactaggac agaacttttt aaattacaaa taaaatagcc
52861  aagtagacaa ttacattagc aagtgatgtt acctatgaaa acgtgaggat ttatggtggc
52921  aatgcatttc agttaacagg gatgtgttag gggacaatgt gagccaatgt agattaagga
```

```
52981   aataagcctg agaaatttat cagaattagc cgtcagtatt caagcactga tcaacagcaa
53041   tgtgtcttaa gggcaggcat cactggtgct gagagaactg ggaattgtca actgtgagct
53101   gctagggggat ggaagaaacc ttagtgtagt cttaggagcc gcttgcttaa acagatgtat
53161   cagaaacata ataggccaag ggtcagccct ttgaaaactg acttcagggc cttcctttcc
53221   tcaggctgct gcctcctagg ccagaccctt attttggctt acattccata acccttgtat
53281   gtgcgatagg gaacctgtat acaatgctga cacggaaagg gaagaccatc gccttttgcc
53341   tttcagtgtc tcatctgtaa gcagggccgc Yggctgacca agatcagttc tgaaggtcca
53401   gcctcttaaa attccagttc tgtgatcaca aagccactgt tgttcctcat cctgccaact
53461   gtgatactgc tgcttcagaa ttactgggtt tcctgttcat catactcacc aacctgaggt
53521   ttggtatttc tcaaatattc tgggcttcca gtacatacta gagcctgtga taatcagcta
53581   atgatcagac aagtttgttg ggagttttac ctaagtattt ttgtgtttta aaaacctagg
53641   gtgggaaatg ctcagagtga gatggtttga cttcattagg catataaccc atttttatta
53701   taaaaagaaa tgcacatata agtaaaaaga ccattttagt tagtcccacc attcgttggt
53761   aaccagttca ctaagtgtac atctttgcag atttctgtgc atacatacaa atatttttac
53821   aagaatagga tcatacatag aatacccact atatggtat gtctgttgtc aatataggtg
53881   ttataattaa gactgtgtag ccttcctctg Kggatgtacc aaaatttatt taattccctg
53941   tcactggaca cttttgtttc actaataagt agacactgtg taagcaatcY gtcaacatct
54001   ctgcacctct attttggta taagtatttc cttaggataa aatcccagaa atggaattgc
54061   aaggtataaa agattattaa cattttttcaa ggctttaaga tgccttacg gtgtatctgt
54121   tacatcctgc ttccacacaa attcttctgt atagccagta cccaagctgc agctctcagc
54181   acaggtgaag acagccagga tgccccagtc aatgctcttg cccagtctgt cagccttcag
54241   gtagtttagg agctgaggca tgacctgaga agagggtgac acacagttag aaagctgctt
54301   cacagcaggg agcacgagac ctctcagcc aggatgatta tagggatctt ggtctttcaa
54361   tcctcatact acaaagcagg attatagaca ttatacaatt aacatgttta acaatctaaa
54421   acttcctat gacttcaaag cccctctcac cttctgttg gtctttccca tttgagaaag
54481   aagttcacaa gtggctgtta atgaattatt ttcattacta atatgccact caaaagggct
54541   gaggcttcta tttgggcaac ttttactttg tatcattgca gatgttgtta ctctttgactc
54601   aagaaacact aattactagt aatgaataca gaaaggacat ctatcaatgt agttatagag
54661   accagagagg aatcttagaa gtagtctaac tcaaagagtg aataggcaga atagcccacct
54721   gatatggaat cactttatac aaatcctgtc acctcaattt ggacattgag agctttggca
54781   ctaagaacca agcagagttt tgtgtatggt cctcataatt ccttttttac ccaaagaaac
54841   aaaccaatat tagctatgac tttggtaagg ttagtgaatc catagctcaa gagcatttcc
54901   accctaccca aatggatttt gatgctaaca aatccttttg ggcagggaag gacatttatc
54961   tttaatgctt atatccattt tttctaacaa atccacaaac caagattaaa cagtaaagac
55021   tcctctcata aagtatatag tcaaagactt taattactag aacaagaaag gaaggtatac
55081   attatttaaa atacaaaag ttaacagagg cactaataat aatgacataa ccacactgga
55141   ggtggagagc aStgtagata tcctcattgt cacagaagtc agtcaatgaa ccgtgtctga
55201   aaactaggaa acagaaaaaa acaagacagt tccttccagg gaactagccc caaggtgagg
55261   caggaaactg atgattttca ttatagggta cccttccata ctgccatgtt gacccatgtg
55321   cacaaattac cttggtgaag tttttaatgt ttaaaaacaa tcatggtgat tacacactaa
55381   atggtcctta tttaaggtca tacctggaat tccaatattc tcttggcacc acaggggcaa
55441   tctggaatat ccttttcttg aggaatattt tcaccagaaa tccagatggg ggcaataacct
55501   ctgccatatc taagaatcta aaatcaatga agatcatgtt caaataatca ataccttacc
55561   tataagttgc caatggtaac atgctatcta ctccatgaat gttcctactc ttgatgtagc
55621   actgacccaa aaggcatgtc acagttcccc catcagacct ggctgtRcca gtgtgccact
55681   aatgccttct caatcacctc aaagtgatta tttcagttta tctgactcag agggcatcaa
55741   aatatatctc ccagatgatg cttttactac ctaatgttgg caacttaatc ctatgaatat
55801   attgtgaagg gactaagaat gagcctcctgc tctaattgca gaattctgcc cagggttctg
55861   gcctaccttc atagttaaaa aattttagga gggacaaata ccaagtgaaa catagtgttt
55921   tgaaaactac tacaaacata agtaaatttc actgtaataa gcttcctaca gcaactgagt
55981   ggttttctgt attttgtcta aaagcatatg cattgctaaa aactgcctta gtgtttaaga
56041   cctagatcta ttcttcctgt gtatttattt gaaccagtga ctggttatgt ggagtttagt
56101   tttctttcgt gatttacgtt tatggtaggg gaggttaagg agaaaaatgt taacatgtca
56161   cattttacaa gccaaagtta cctgttggaa atgggcaaaa atacccttt ttctttctgg
56221   cgggggggcc aatggtgcct aaacctcatg taccttaggc aacatctcat tcatctccca
56281   tccctgatgc ttgctttaga aaatgaaccc tgtatgataa acagtataac cttctagtctt
56341   ttagtaacta ttaaatggat cagcactgca aaacaccttt ctacatggcc catctgtgtg
56401   aggaactcct ctaacaagat aacaaaagcc tgcttttata ggctcctaag gaacagacta
56461   atgttactat gaagttatt cttacagatt atactcataa aacatggcct gaagagaaca
56521   cgatgaggag ctatgagctc cactttacct gttctggttc aaggctatc tgagttttaa
56581   acttctgaaa aattttatct tccctggatt catgttttgc catggaatcc agttcttcct
56641   caagtgcttc acctgaaaaa tcaacgtaac tattatgaaa aacaggagta atccccacaa
56701   cttgacaatt cacacatgga gaggggaccc actttaatc agatagcttt ccctatttat
56761   tcactcattc aagttggacc atctgaattt ccaggtactc catccaactc tattatatgg
```

```
56821   acttccattt agtgcatctc cttaaagctt caaaataaca gaatggtcaa gggcttagga
56881   ctgcccagca catcacagga cacccaacaa atgtgagccc ttatcattag tatcctcagc
56941   tggtaggctc actcactcag tcatcaagtg ttcatttctg gcctggagca gtggctcacg
57001   cctgtaatcc cagtactttg ggaggccgag gcgggcagat cacctgaggt caggagttca
57061   agaccagcct ggccaacatg gtgaaatccc gtatctacta aaaatataaa aattagccag
57121   acgtggtggt aggtgcctgt aatcccagct actcgggagg ctgaggcagg agagtcactt
57181   gaacctggga ggcagaggct gcagtgaacc gagatggtga cattgcactc cagcctgggc
57241   gacagagtga gactccgtct caaaaaaaaa aatgttcatt tccttctcca cattccttcc
57301   tgggattaca gccaccctaa gccactgctg tccccaacag acccgtgtct ctaagtataa
57361   ccattagtct ttgtaatgta cgttaaaata gaactgatat accttgggtc agagaagcta
57421   aaataactgc tttgatgaaa ctggaaaggc actgatggtg ttcacttgca ccatcaggtc
57481   tgatggagga agtgtaggat gccttcagat tgatgttcca tcaagtatac gtggaaagtt
57541   tcagtataac cgttaggaca ctgtaaatgc tgttccctca ggccctactg cctcctgcca
57601   agtctcaggt aagacacagc tacctccagg aagcattttt ctattcaatt ctccttttat
57661   tttagaaaat tttggacata cagaaaagtg gaaatactat aatgaaccgc cacatatcat
57721   taatcagttt caacactatc aagtccagtg tttcctttct ctgccacttc cacctccatt
57781   actctgaagt aaattccaca catatcactt cattcataat taagttatgt accсctcgaa
57841   ggcaaactct ttccttttat ttaccaattt gaaaatgagt ctgttcccaa gtatcctata
57901   aagatgatta ctgagttttt ttaaagtatc attttgaacc cattaaacat atctgatgca
57961   gttagcgtcc ttgtggatgt tcaaactgtc catcttttgc aagcaggagc cttttcatgt
58021   tgcttgagtt ctgacatggc cctagtaatc cttatcctta atctttgata tgaccatgtt
58081   cccacattat atgaacgttt cctgacctag ttctggaatc aaccacctct ccaaagagcc
58141   tggagttcct tttagagaga aatggtacgt agacacaatc aacattatct tcctcctacg
58201   cccaacatct cagttctcag taacaccaac ataattactc gtttcctttc cccccaatac
58261   acacacaacc atctcaaaat aaaagcaaca gtctagtaat aacatgttta ttcaaaatac
58321   taacactgtt acattctttt cattctcagg gcatattcta ctagagatgt actgtcctat
58381   gttttgaagt cacctggaag agttcttagt gtggttatat gactacatca agagtttttt
58441   acttttgatg attagggact gctttttaaa acttacttta ctccataatc ttaaaatact
58501   catacagttc cacagtcaca tttacactaa caaggcatat ttgaagtcca gctttcatcc
58561   ttgatcctgc tactctaggc tctccttttct cctaaagata agcattttca ttatgtatca
58621   tgtttatcgt ataggcatga acacacgcgc ggccccttcc aggcagtctt cagtgatgtc
58681   acgtgttccc atggcacctg tattgtactc ttatcagtca ttatatggac tttaacttcc
58741   ccagatatta tttgggctcc tccataagac tgtgagcatc tgaccactgg agtgttgctt
58801   cccattatat ccctgttatc aagcacaagg tcaggcacag agtaagactc aaaacatgtt
58861   ttggaatgta tgactggtat gaactacaaa ccagtaagct gatgttttca ttttgagtct
58921   ataaatctaa ttttgtggtg gttttgtgta tKgctcaagg ctcaaattgt aaaatttaat
58981   attatgtgac caaagaaagt tatacccaga acctcaattt cctcaccttc aaaatggggc
59041   agtttctcac tcattggtct gctgtcacga ttttaatgag ctcatgcaca aacagccctt
59101   tatataaggt aagtgctgga taaatgttgg ctactataat aaaataagcc tctaagatac
59161   ttggtcagca caagtactac ccaagagtat gcactgtaag taaactgaca aaattgtgta
59221   tctaaaactg gccagatgaa agagaaactt ttaaggggcc cttctgcgtg cccgacactg
59281   tgctaggcac tcacactatc ccgacccgag aaacMgatct gcgacccaga ggaacttacc
59341   aagcctccag catcttgtgc agccctactc atgggaccat ctggataccc acccttgtct
59401   ttacagggag cagaacacac ctcttatgtg tcagaaaaca aagtccagga agtatatttt
59461   tacctgaggc aatatctgaa aattgtatgc tacagcctcc aaagtgagtc ttcctctcag
59521   tacctctctt ctaggcacat ggagcccttt cttccaagta ttatgtttaa ccacttaatg
59581   aatgaagtcc tgaaactgct tacccatgct ccctataatc tctgagtaat cttccttttc
59641   cacaacctca ggcataatct catcttctgt ttctattaca atttcaaatt ctggaaaaag
59701   gaagttgtgg tctggaatta tatggtccag atgatctgaa acaaaaagga cagcactatt
59761   agtaatcatt tagttttgaa gacagtctaa taatttgctg tctctaaagt actatattcc
59821   ctatagttct ggcattttag ataaagggtc ataaattaaa tgcctatatg gtgacattat
59881   tcagtgattc agacttcaca gccttttttt ttttttaca aaggtgttcc aggcatgaaa
59941   aattttaaag tactatacct ttcctaattt tacctttaaa gttgtcctgg aaatatctgg
60001   gttgacaaag gcgatgaaac tgaactgaRa cttaaaaaaa agattaccca cctggttgtg
60061   cacaagcctg cttatgtccc aatctccagt ctagggtctg atgctccttg ctgcagtaat
60121   atgctttgtg gcatctggag cacgttttgg ggcctaaaca gccacaaacc ctgcagagat
60181   gagcaccaga cttaagctgg agacacactg attctcctgt ttctgggggga ggattctcag
60241   aaggtggctc atatgagtaa aaatcgtttt tcctgggtag ttgattccta aaaactaaaa
60301   aagaatacag agaaaagttt tatcttcaaa caaaacagca attcacatat tttatcctct
60361   gcacgtaaaa ctgaaaataa caacaacaaa aaagaaatga aagtttttgc tttcaggaat
60421   aagcttttaa aatccagaaa ctagatttcg tccggtacac gcaactgagt tgcctcctag
60481   aggtggtttg agttaatcaa attaataaga ctgatcgtta agaacgactg ccaaaaatac
60541   gaaaaagcta ctgggatcca tctttccaag acaatttcta ttatctgaat taacaccata
60601   cctggtaccc actgattaaa agctggggt taccaatgcg cgtgggcaca gttagaagct
```

60661 tatgtagcaa aaatgagcac atcctggaag ggcccgggag aaggtgctcc tggggcagcg
60721 cggagaggga gctctgaggc tggggcggca gcggtgcttg ccgccgtccc cctggtcgct
60781 cccggaatta acgccgcgca cgcgtcggag gcatggcccc gtcccgaccc cgtttggcgg
60841 ctcacctcgc aggccggcac agcacggctg ctcgcggcag cagaagagga agatgcagcg
60901 gtggaaggcg tccgggcggc caggcagcgg cgcatacacc tgcagcagga aggagagcgg
60961 gcggccgcac agctcgcagg ccagggcctg gggccccggc agcccggccg cgcccagcca
61021 tgccggccgc ccgcccacct tgctggggaa ctgctcgctg cgcagtcgcc acgccggcgc
61081 cgactcggcg aagcccagct ccacaggcct ggccccggcg gcagccatgc ggggcgcggg
61141 ctggcgtggg gcgcagccca cagctgggtc ggaaggcgga aatcgggcgc cgggccggaa
61201 ggcaagaggc gggcaccttt ccggaggaca ggaggcggaa acgcgtctga cgggagcggt
61261 tgcaggacca atgcgaggga acggggcaga ggaaacctct cggcatcagc cccgcccctg
61321 gcgcctctgc ctccgagccg ctttcctggt gcctccgggt gctctgggat ggttctggtc
61381 tttgggagag tggcagctgg tgacggcgct ccgctcacct ctgcacatgt cttgctgtgg
61441 gcctgcgggt ggccgccagg gaggcagagc cctcccKcaa accttccctg ctggtgtcca
61501 cctcagggtg tgggaaacct gtgcgctggc cgagtgctaa ccaagagtag gcagtgaaag
61561 acaaatgaag gttgaacagg taaagtgagg accctacagc ggaaaccaag aatcctgtgt
61621 gcctgagagt aatgaagaag cctctgcaga agagtctttt ctgtcagtct taaggtctct
61681 gttttaatgt tagtgctggc ttgctgtacc tgaattccaa gggaggagtg tataatgagg
61741 catggccaac ccccacttcc catcattgcc tgaactagtt tttcaggtta acttcagaat
61801 gcccttgggc aagcagaggg tccatcagtc ggttggaggg tttagaattt tactgttggt
61861 ttgcaaaggt ctgaaagaaa catgtaccac ctgttctctt taaggagttc tacttaggag
61921 gtttcattta cataacaaga ccgtggttgt cagccaggtc tccacccgca taacctgtta
61981 tgccacaatc caaacccccca ttctgtaacc tcaagatggt atataagttt ctgaacccca
62041 tttggggctt cagcaaaatc actctggttc tccccccatgt gcatgttaat aaatttgtat
62101 gccctttctc caattaatgt gccttttgtc agttgacttt tcagtgaacc ttcagaggac
62161 aaaaaggaag ctttcccttg gctactacag tggctttaat ggaagtaaag tcatcaacaa
62221 catttatttt tgacaaaatc acagtttagt tggcagtata tttgtttgtt tttgttttat
62281 ttgagatgga gtctcgctct gtcgcccagg ctggagagca atggtgcgat ctcggctcac
62341 tgcaacctcc gcctcccgag ttcaagcatt ctcctgcctc agcctcccga gcagctgggt
62401 agcagtatat ttgtaatggt acataaaata atgtctgttt ttaaataaac atttacattg
62461 taaaccaaaa gttaactctc catcaatttt tttttttctt ttttgagatg gcatcttgct
62521 ctgtcaccca ggctggagga gtgcagtggc atgatctcgg ctcactgcaa ccttcgcctc
62581 ccaggcaagc gatcctcttg cctcagcctc ctgagcagct ggaattatag gtgtgtgcca
62641 atacaaccag ctaattttcg tatctttggt agagacagag tttcaccatg ttggccaggc
62701 ttgtctcgaa ttcctgacct cagttgatct gtccgtctca gcttcccaaa gtgctgggat
62761 tacaggcatg agccaccaca tccggcatcc atcaatttag aaagtttatt tcaccaagat
62821 taaggttgca cccgtgacac agcctcagaa ggccctgatg accatgtgcc cttggtggtc
62881 agggtacagc ttgcttttat acatgttagg gagacatgag acatcaatca gtatgtgtaa
62941 gatgtacttt agtcaggtaa agcgggactt gaggtgaggg cttccagRtc atgagtagat
63001 aagaggcaaa agatcgcatt tttttgagtc cttgatcagc cttccactga atacacaatt
63061 tagtctggct cagtgaatta tcatttttaS gtaaacaata ggggaggggga agcaattaga
63121 tatgcatttg tctcaggcgc accttaaagg gataactttg agttctgtct gtcctttatc
63181 cacaaggaat ttccttgtgg gcaaatttta agggaggtac gtagcctctt atcttggcag
63241 ctatcttatt taggaataga atgggaggca ggtttgcctg acatagtttc cagcttgact
63301 ttaccctttg gtttagtgat tttgtggtcc tgagttttat tttcctttca cagaaattat
63361 accgtaaaag taattgaaga aaatcacttc tttccccttc cctcaactag gccttgacca
63421 ttttaaataa aatcaggatt tgctgaaggt caacaaattt aaccaagttc agttaaaact
63481 taactctgaa tctgtatgtc cctggggtct tttccagtga gagatgtcta agcatcattc
63541 caagcttttc tatactaact ggcctatttg tatgtttctt attttaggat tccttttgtt
63601 catgtgtatt tttattaggc aatcacccat ttcctgtagg tttccaggtt aatatatttt
63661 tcttattgga attttaattt atcctctcta gtttctaca tatttttttt ttctttgaga
63721 cgaggtctca tatgttgccc cggttggcct caaactcctg ggcttaagca atcctcccac
63781 cttggcctcc caaagtgctg ggattatagg tgtgaattac tgtacccagc ctagaatcct
63841 tagtcctata tacttttgct gttttttca ttgccaactt gaaataataa aaagggtcag
63901 aatcctataa accaaaaata aaataaggcc ccccaaccct ctgaatggac ttcctcctct
63961 gacacagatc ttttacaatt taacctgtat gaaccccaaa aattggagac aggtctcagt
64021 Kaatttagaa aatttatctt gcgaaggtca aggacacacg attatgacag cctcaggagg
64081 tcctgacgac atgtacctaa gatagtcaga gcacagggtg gttttataca ttttagggag
64141 atataagaca tcaatcaaca tatgtaaaat gaatattggt caggaaaggt gggacaactc
64201 aaagaaaaaa tgggacaact cgaagtgggg aggggcttcc aggtcacagg taggtgagag
64261 acaaatggtt gcactctttt gagtttctga ttcacctttc taaaagaggc agtcagacat
64321 gcatttatct cagtgagcag agggatgact gaatggaatg ggaagcaggt ttgccctaag
64381 cagttcccag cttgactttt cccattagct tagtgattat gggattccaa ggtaatttcc
64441 tttcacattt cccccctttt cttttttaaa atattttgga gaaagcattt ttgaagaaaa

64501 taagtttctg ttcccaggtt ttatctgctc tctcatggct aggatggttt tttcctagaa
64561 gggtaggtcc tgagttatta ggaaagctca tttttagaag gttgtgaagt ctaatatcct
64621 atcaagagaa aatttgggga ggaagggaga acaataagaa caatcttgga aaattgatct
64681 aggccacatt actctgaagt ccatacatca gtaagcaggt atgaaagtgg cttatgtatg
64741 taaataggtt cccattattt tcttctgaag tttaagttgt ctacttcagt tcacagggct
64801 tcacgaaagt tagttttaag tgacttagtt tagtgacagc ttagttttaa gtgactccaa
64861 attaggaaaa atggggaaaa aaagaaggaa aaaaattgaa aacattattt tgaagacttg
64921 tagcccacaa aaattagaat ttggtccaaa ctgtagaaaa tgataaaaat tgaaaaacat
64981 taggcaagac tagaatctaa caactggtgg actatagttt tccagtctct agtttcccat
65041 ttatactaaa gacaaatcat gataggtttg ccttattata tttggccgaa ttatttgtat
65101 acagtgcagc aagaataatt atttttttaac attggctttt aaattggctt tgatggaact
65161 ttgttccata gagggtattt cagataagac tttttaaaag ctgagcccag ccatggattt
65221 gtgcccacaa atacctgtga gtttggtgat cctctcctct tgaggttcca agataaactt
65281 gaggctcctg ggcctgtcag aaagtgacat tctttactta ccacaggtca ggaaccctgt
65341 acaggagctg tgtagacaaa gttatgagga cggttttcc aaggggttt aattggctcc
65401 gtaagtcaag taaaagcatt ggtaaacaac cagtttcccc aattgtgtcc tgttacaaat
65461 gaaaacagat tattagtgca cttatgcaaa taactgtatt gtcataagtt aagaatactt
65521 acagtttcca aattctggag aaatcgggta gagagaacca aatgtgctcc aaattttgtt
65581 cataggagta tgtgttactc aattgttaaa agctgcagat agcctgacca acatggtgaa
65641 accctgtctc tactaaaaat acaaaaaata gccaggcatg gtggYgcgca cctgtactcc
65701 cagctacttg ggaggctgag gcaggagaat cacttgaact tgggaggtgg aggttgcagt
65761 gagccgagat cgcaccgctg cactccagcc tgggcaacag agcaagactc catctccaaa
65821 aaaaattatc ttgtttttat caatctttct taaatgtata gctcacattt attttcaatgt
65881 ttaaaatgag aaatatttgg ggtctttatt tagacgtttg ttgatgtttt tgtgaccaga
65941 aatatgttac aagaacttaa ctcttgttta tatcaatcat cccatggcaa attggtttta
66001 ttaccagtag tgttgcttaa agtcacagtt tccaagaatc tatccatgat aaatggaggc
66061 ttactggact taatagtact gaattgtaca cataaaaatg gttaagatga taaatttttat
66121 gttatgtgta ttttaccaca atttttaaaa atgaaaaaaa gaaatcctgg ggaatgatat
66181 gttcaaagaa ggctttgaaa agctctgata tattccagaa atctagacag ctacacaggg
66241 gcagggcttt gtgcgtggcc atgaagagcc tgaggcagct gtaatgtttt acatttgact
66301 ctggggttct gtgccatcag aaagtgaagg ctaaagcaga cttggactgc cagagtgttg
66361 aagatgtgtc ccagcacata caaagccact ctacaaaggc tgggagacat aggttcaagg
66421 catttaagga aatctctatc taatcattag ctgaccactc agcacactaa gcaaagactg
66481 aaagacacat gacaaagaat acagacttca tagaattagt cagggaaagt cactaaaaaa
66541 ttcaacagca acaacaacaa aaccctgag agggaagggt ctggcttaca gttaccacat
66601 cctagtcttt aaaatatcca gtttggcca aaaatatgag atacacaaag aaacaaaagc
66661 ccatgcagag gaaattctga gaccagctcg atcgggggag cccttaaccca gtggcactag
66721 gggatattaa agacacacac acacaaatat agaggtgtga agtgggaaat cagggtctc
66781 acagccttca gtgctgagag ctccaaacag agatttaccc acatatttat taacagcaag
66841 ccagtcattg gtattgtttc tatagatatt aagttaacta aaagtatccc ttatgggaaa
66901 cgaagggatg tgccgaatta aaggaatagg ttgggctagt taactgcaac aggagcatgt
66961 ccttaaggca cagatcgctc atgctattgt ttgtggctta agaatgcctt taagcagttt
67021 tccgccctgg gcggaccagg tgttccttgc cctcattccg gtaaacccag agccttccag
67081 cctgggtgtt atggccatca ggaacatgtc acagtgctgc agagattttg tttatggcca
67141 gttttggggc cagtttatgg ccagattttg gggggcttgt tcccaacagg aaaataaaga
67201 agtcaatgga aattctccat gaggaggccc agatgttatc cttcctaggc aaagatttta
67261 aattagctat tataaatatg ttcagagaac taaaggaaac catttctaaa gactaaagga
67321 atgtataaga atatctcacc aaatagagaa tactaatgaa gagataagaa ttagaagcac
67381 caagtaagaa atgctagagt tgaaaattac aaaactgaaa tacaaaattc gctagaggca
67441 ctcaacagca gattagagat tgcaaaagaa agaaacagca aacttgatga taggtacatt
67501 gagattaccc aatcagagga gcagaaagaa aaaagaataa agagaaatga acagagcctt
67561 agaaatctgt gggataccat caaacaaatc tggaagtccc agaggagaga acaaggggga
67621 aaaaaggcag aaaggctatt tggagaaata atagccaaaa ttttccatta agcttttcat
67681 ttgattaaaa tttatatatt ttaaaaagtt taagtgtatc ctactcatac tttttaaaga
67741 ggtccatacc tagacacatc atagtcaaac tgccaaaaaa gagagagaga atcctgaaag
67801 caccaagaga aaaacaattc atcttgtata agagatcatc agtaagatta acagctggct
67861 tcttgtaaaa aactcacaga gaacaaaatg ctgcagaatg acatacttgg gaaggcagtg
67921 gggtggagaa gcatgccaac taagaattgt atatccagct aaactagcct tcaaaaacca
67981 aagaagaaaa ataaaaaaaa aatgagatat tcccaaatta ataataaaca aataacactg
68041 agataatctg tcattcatag atctgcctta tgagaaatac taaaggggct cctctttcag
68101 gctgaaataa aagaacatta cacataactt gaatctacag aagaaaaaag agcacggtta
68161 aaagtaacta cataggtata taaaaatgat agtatcaaatg tatttttgtt tgcttgtaac
68221 tcattctctc tgatttaaag gacaactgca ggaaacaata ccaatataaa tgttttgaca
68281 atgttatatg aaaatttaat ttgcatgatg gtaataccac aaataagagg gatgggaata

68341 gagctatatt ggagtaaagt ttttgtgtat gatttgaatt aagttggtat taatcctgaac
68401 tagattgttt taaatttaaga tgataaactga aattaaatgt taattgaaag gcagtcacta
68461 agaaaatagg gtaaaagaaa caaataaata aaatggcact taaaaatatc taacagtaaa
68521 gaaagcaata atggagagca aaatgacttg aaacatacag aaaataaaga gcaaaatagc
68581 aggcacaaat cctaccatat cagtaattaa atgtaaatga attaaacatt ctaataaaaa
68641 aggcagagat tggcaaaatg gattaaaaca caaaacacag acagaacag caaccattct
68701 ccaattatat gaggagacct gctttacatt caggaaaaca aataggttga aagaaaggga
68761 atggaaataa atatactctg caaacagtac ccaaagacag ctgaagtggc tatataaaca
68821 ccagacaaaa tagactttaa tgcacgaatt attagagaca aagacatttt ataatcaaag
68881 ggtcaatgta tcaggaagac ataacaatta taaacatata tacctctgac agtagagcac
68941 caaagtaaat gaaacaaaaa ctaacttaaa aagagaaata cacaggtcaa caataaatgt
69001 tggagacttt aatatcccac tttcaataat gaacagatct aggcagaaga tcaacaaaaa
69061 atagaagact taacactatg aaccaaatag acctagcaga catctgtata atactgcatc
69121 caacaactgc acaatatata ttcttcaaat acacatgaaa gattctctag gatagaccat
69181 gtgttaggcc ctaaaacaag tctcaattag tttaaaagga ctgaagtcat ccaaagtatg
69241 tcttccaacc acaataaaat gaaattagaa atccataaaa gaagaaaatg tgagaaattc
69301 acaaataagt agtaatgaaa caaaataacc tatgggataa aaaggaaatc acagggggaa
69361 ttagaaaata tgtagagatt aatgaaaata caccatgtca aaatttatgg gacacaggac
69421 agtgttgaaa aggaaattta cagctgtaaa cacctatatt taaaaagaaa gattttagtt
69481 caataatcta aacttctacc attagaaatg aaaaaggaaa tgcaaacaat ctaaatcaag
69541 cagaaagtag aaaatagcag agattagggt ggaaataaat ggaagaccca aaaaacagag
69601 aaagtaataa aatcaaaagt tggttattgc cgaaaccagc ttggctgggg agaccctaac
69661 ccagtggcac tagaggaatt aaagacactc acacagaatt atagaggtgt ggagtgagaa
69721 atcaggggtc tcacagcctt cagagctgaa agcctcaaac agatttaccc acatatttat
69781 tgacagcaag ccagtgataa gcagtgtgtc tatagattat agattaacta aaagtatttc
69841 ttatgggaaa caaaggggatg ggcggaaata aaggggatgg tctggctagt tatctgcagc
69901 aggagcatgt ccttaaggga caqatcgctc atgctatttt ttgtggttta agaacacctt
69961 taagtggttt tccgccctgg gtggtacagg tgttccttgc cgtatttccg ataaacccac
70021 aatcttccag catgggtgtc atgaccatca caaacatgtc acagtgctgc agagattttg
70081 tttatggcca gttttgcggc caatttatgg ccagattttg ggggcctagt cccaacgtgt
70141 cccccttctt tgatttgcaa agtgataaaa gcaaaggcag ttttgtcacg gtgagctact
70201 tcttgcagga gtcaggatcY gcatctgcag actatacaaa aacaacatag attaaaagca
70261 caatcatcat cgaaatcaca gagcttccaa gtgttttcat ccatttaat gggttgctag
70321 ctcKttatct gtctgcagct cctttaagca ctccttttcc tggcattaag gtcagtgtg
70381 cctaggatgc tttatttgtt cttttaattt tgcaatatcc aaaaacaagc ttgtagagtg
70441 tcctttctaga tgcttttaa attcctctcc aaatttgat ctaattaaga gctattaata
70501 atttccaaca atccttattt aagcttcctag agtcggccat atcatttgag gttgaggtgc
70561 cactataccg ccatggttcc agatgatagg aactcttgcc atgtcttatc atttctacca
70621 tctgaccatt ttgttcagac cagctgaaca tagtgtggct gtggcatgca gactgagagg
70681 tgcaattcaa gccaaacatc cccttagggg accaatcaat aatgattcca taggaagcat
70741 tgtgcagcac ctctgcctgt tctgcaatgc agtcttccta aacaagtaca ttcatttttt
70801 ctaactgggt ccaatcctgt ttacaaatag gtttttgagg gcagtatgcc ttaattatag
70861 gagcagattt attatggtaa atactgagat cagaaagcat gtgtaagtgt gtcatagagt
70921 gattacatcc aggcattatt gccagccaag attgataaMt atgcccaata agtacagttg
70981 ttctctgtgt cagcacttgt tgaaggaata ctcatggcaa tggtgatcac cgctgtcata
71041 gctaccatta aattactcac tgtgactggt tgtcctgctt tcctcaggtt ttctttctgcc
71101 aactgtgaca gcttcttgat ctgtcccaa gtgggtggct gtgttgatg ggtgttgctc
71161 gtgacagttg gggtcctcct cagcatcagt cttgagatgg ctgcaaccag gggtcctca
71221 ggatcctcct ggaatctctt cctcagcatc tggctcatga taaggtttca ggtatcttga
71281 tggtatccaa atcagctctt gattttggcc tggagaaaca caagcataac ctctacccca
71341 agttattatt ttacctattt cccaaccttt tgttatgcaa agtgagaaaa ggtgtgcaca
71401 catacatgta acgtgtgaca tccatttgcc aaagataatt aggttccaat cctcgaggat
71461 taactcctcc tgcaaaagat gaggaatgca ccatttggca agttgggcat cactggatca
71521 taactttagc ttctttccag gtaatgctgt atctgtgttt cagaccagag gcattaacat
71581 gggttaaatt gtgaaaatgt ctagcagtag atattgcttt agcaactagg tgatcagcca
71641 tttgattccc ttcagtcaaa ggtcctggaa gaggtgtatg agccctaatg tgagtgatgt
71701 aaaaagggtg cattctactc ctaactgctg tttgcaactg ggtaaataaa gtcattagtg
71761 tcatctgttt gaaattgtaa ctgagcattt tcaactaact gtgtggaatg aaccacgtat
71821 gaagaatcag aaatcatatt aatagacata ttaaaagcag tcaatacctc aattacagct
71881 acaagctctg ctgttagagc tgaagtataq ggtgtctgga aaacttaac ttttgagcca
71941 gaataagaag ctttaccatt actagaccca tctgtgaaac aatgaaaatg cttagcaggc
72001 tgcaagttgt ttactgcagg aattataaat gtaaaccatt cacagtcttg cttagctaaa
72061 gtgatagtaa agaaacagtc ctttaaatct gtgacaatta aagqccaatt ttttggaatt
72121 atagcaggag aaggcaatcc aggaggctgt aatgctccca taggttgtat aactgaattg

```
72181  atagctatta agtcagttaa cattctccat ttacccgatt ttttcttaat tatgaaaact
72241  ggagaattcc aaggggaaaa tgctggcgct atgtgcccat tttctaattg ttcagtaact
72301  aatrcctcta aagcctccag tttctcttta cttagcggcc attgttctat ccaaattggc
72361  ttatctgtta agcatttaaa aggtgtaggt tctggaggct taacagtggc cgccatcaaa
72421  aatgatatcc tacaccttgg cgggaacttt gtctttacgc ttgaagcggt tccttcaaac
72481  cttgcaattt ttttcctagt cccataccag ggacatgccc catttcatgc atcatatgtt
72541  gactttgagg gctatataat tgttctggaa ttagaacttg tgctccccat tgttgtaata
72601  aatctcttcc ccataaattt gtaggtacag aagttataat tggttgaata gtcccaggtt
72661  gtccatcggg ccttcacaat gcaaaatata actactttga tatacttcag gggctttacc
72721  aactccaact atgttaaatt gagcgggtgg aattggccac gcaaacagcc agtgctgtag
72781  agaaatgatt gaaatgtctg ctcctgtatc taccaaacct ttaaatttct ttccctgaat
72841  agttatttca caggtaagat gtttatcagt aatttgattt acccaataag cttctttgcc
72901  ttgtttattt gtgctttcaa atcctcctgt tcgtttaatt taacttttcc gtatttctac
72961  atacggcaca atcaggagct gtgctataag ctctcctggc tctgctttcc agggaacaga
73021  agtggatata acaatttgaa ttccacatt gtaatctgaa tcagtgactc ctgtttgtac
73081  ttgtcatccct tttaaattta aactagacct tactagaagt aatcctatca tccctgctgg
73141  caatggtcca cagactcctg ttgggaactt ttgtgggggt tccccaggca gaaggctcac
73201  agcatttgtg cagcataaat ctactgcagc agtaccagct gtggcagggg acaaacattg
73261  taaatcccat gaagtatatg gggtattagt gcattcattt agagctgagg gctcttaggt
73321  ggaagatgtt aataaactgt ccaggtccca tggttcagca gagcattttc cattgctggg
73381  gccctaggg atctccagga tttatcccag agtgcccata atggacagta caaaaStggg
73441  aagagtttcc aagaaagcaa atacccccatc atccaccaca aaacacactc tcagcttatt
73501  catcaatgtg gcactggggt ccttaatgtg tggcaggcag aggtaatgac agtgagcaaa
73561  tagcccaggg attacttgag ctaaaagcaa caaaggaacc aaacgcttcg actttctgac
73621  caaactcagt tcccaactga agctggtctc atgcaagtgt gctggcctga gtgatctcac
73681  atcctgtgaa ggctctgcca aggagggatg gtggctaggg tcaggcctcc ttaagagggg
73741  tcccggatcc taccagaggc taaggtggga ggatcggttg agcccagaag tttcagagca
73801  gcctggacaa catggagaga ccctgtctct gcagaaaaaa aattagcaga gcatggtggc
73861  aggagtgttt aatgccagct actcaagaag cagaagtggg aggattgcct gagcacagaa
73921  gtaccaacct gcagtgagct atgattgtac cctgacactc cagcctgggc aagagagtga
73981  gaacctgtct caaataaaga aaggaagaaa ggaagaaagg aaggaagaaa ggaagaaagg
74041  aaagaaggaa ggaaggaaaa ggaaaaggaa agggaagaaa aagaaaggga agcaaaggga
74101  ggaaggaagg aaggaaggag aaagaaagac aaacagagaa aagaaagaaa agaaagaggt
74161  gctttggaga aacccacaga agacttttac actttagttg tgttttgaat actaaatcc
74221  aacatacaaa ggaatagaaa ttatattctt cacaattatg attttttctt tctttctccc
74281  ttttttttt tttttgagac agagtctttgc ttcttcgccg aaactggagt gcattggtgc
74341  gacctggct cactgcaact tctgcctcct ggtttcaagt aattctccta cctcagctcc
74401  cccagtagct gggattaaag gcatgtgcca ccacacccgg caaatttttg tatttttagt
74461  acagacaggg tttcttcatg ttggtcaggc tggtctcgaa ctcccaacct caggtgatcc
74521  gcctgcctcg gcctcccaaa gtgctgggat ttaaaggcat gagccaccgt gcccggccag
74581  gtctcgattt ttttagaaag tttattttgc caagttggag gatgcgtgcc tgtgatgcat
74641  cctcaggagg tcctgacaac atgtgcccaa ggtggttggg gcacagcttg gttttatata
74701  ttctagggtg acatgagaca tcaatcaata tgtgaaagat gtacgttggt tcagtccaga
74761  aaggtgagac aacttgaaga gaaggccaaa cagggggctt ccaggtcata ggtagaaaag
74821  agaccaatgg tttcattctt ttgagctgct gattaccctc tccaaatgag gcaatcagat
74881  atgcatttat gagcagacag gtggctttgg atagaatggg aggcaggttt gccctcagca
74941  gttcccagct tgacttttcc ctttagctta gtgatttgg gtccccaaga ttgattttcc
75001  tttgtaagg tctaacatgg ttcctcatga gcatttaatta ttcattgtgt atttattac
75061  aaaaataagg cacagatttt ttaaaaaaca tcaatttcat gactagttat atacacataa
75121  ttacactgaa gttcaactaa atttggaaac attccagagt ttgggtttct aataattctt
75181  tgtgattctt tagaagctaa aatattttaa caaagcaaca tctaaaatca cctgtagaat
75241  gtcctgccat ttttgtttct ctagtttcct catttctgc aaagcctcgc tgaggaaatt
75301  gactctgaat atcctttac actcttctgt tttagaaagc attgtggtga aacattgaat
75361  catgtggtc acaagttctg ttcacattct ttctttcttt gaatattttt tcccagtggc
75421  caatatttga ttctgttgta ttatgggtaa aaggtaggca tgagaacaaa ataaagacaa
75481  gaggtctttt gaataagtga tccagtcaca atgaatcaat ttgccattgg aacatatttt
75541  tacgtcactc ttctgaaaat atttagccat gaattgaaag agagtctgta agattatttt
75601  tttcctgttc taaggtgaac agcatttag agaatgaacc acaaccacag cacaagaaaa
75661  aaatctgata aataagttta cacatatgtg ttactactgt aacatagaaac atgtaaagag
75721  catttgtttt gatttatata tcagtctgta ttgtttaatt ttttgtgtca taaatgctct
75781  tatttaaaag acaggactat ttaacagtgt aaattactag taattcatgg tataaataat
75841  taaacaagga agtgttcaaa aatataacaa tgttttaaat aagcccattt tgtgcttctg
75901  taacagaata cctgaggctg ggtaatttat aagtaaaaaa cgttcatttg gttccacaata
75961  ctggtggttg gaatgtctga gattgggcag aggcatctgg tggggcctca gtcttttta
```

76021 cctcatggtg gaaagtggaa ggggagcaag ggagtgcacc agagatcaca tagcaagagc
76081 aaaagcaaca gtgaagccaa ggaagtcaga ctctttttaa ctacctactc ttgcaggaat
76141 taatccattc ctgtggagag agaactcact caccctctgtg gaggacaata atctattcat
76201 gaaggatcca tcccatgacc caaacacctt ccactaggcc ccacctcccc acactgccac
76261 attgggggtc aaatttcaac atgagatttt gcagggacaa accacatcga aaccttagta
76321 atttgtagca tagttaaatt ctttttcaca tgatgtattc tgtgctggga tactccacat
76381 cctgaatatt ttaatttaat ttgaatagag tttgatttac ccattttgct gtaaaattcc
76441 gtgtgtttta acaaatgcat agttgcaggt atccattatt aaagaatcat atggaatgct
76501 tcaaatcccc accccatgca gccaatggca ttcccatctg tgcagtttgc cttctccaga
76561 atctcattaa atgaggtcac actgtgtgtg ttctcctcag actgtcttct tccactcagt
76621 aatgtgcatg caagatttcac tcatgtcttt gtgtgagttg atagcttgtt cctttctatg
76681 gctaaatagt attccattgc atgaatgtac cacaatttgg ttatgcattt tagggagcaa
76741 aaccttcctc ttctaacttt gttccagggt tggagacctt caaattaact gacaatagat
76801 acattagtag gagaggcaat acttgggctc ttattccaca agtatcattg tgggacaaaa
76861 ttcatcagat ggcaggatct agtttacaaa gaggtgaaaa tagcccaaaa cgagaaacaa
76921 gactagaatc tgataaccca caagggctat agttttcctt tttaaaaaaa ttttttttg
76981 agacagagtc tggctctgtc gcccaggctg gagtgcaatg gtgcaatccc agctcactgc
77041 aacctctacc tcctgggtgg aagcgaacct ccctcctcag cctcctgatt agctgggact
77101 acaggcacat gccatcatgc ccagctaatt tttgcagttt tagtagaggt ggggttttga
77161 actcctggcc tccaaaagtg ctggaattat aggcttatgc caccatgcac ggctgagtta
77221 tagttttcca ttgaaacata aaatttctct ctgtagtaac catcattttt gatcatagat
77281 aatcaatgtg agattattct tgttttaaaa ataagtctag tttcgttaga ttttgcctga
77341 gtatttatgt aagtgcagca agaacaggag gtgaccacgt aggtgctttc aagcttcttc
77401 gctggaagtt ttcatacaga atctcagatt ggactttaa aggcctttatt gaggctaaaa
77461 gccaagccaa gaacatactt tcaaatttca gtgcagtca ttgtagcttt atgtgaattc
77521 ctctctctct gacgcccca aaatatcccc aasttcctgg gcctagcagg aaattacctt
77581 ctttactaac ctgtaaggct gtgaaccgtg taatgtaggt accaggctgg cttttctcaa
77641 agtgctttgt aagcattggc ttcataaaag tcagccttag ttcctgaaca ttgctggtca
77701 taactgatct caggtatact attcctaaat atgatattcc agtaaaagcc tgataatata
77761 atcaaagttt ccaattatgt cttgctataa ggtgaacaga tgcttattgg actttctgcta
77821 acaactatat tgtcatgaaa ataagagtat tcagtaagat tttcaaaatt ctggagaaat
77881 caggcaggga aaaaaagatt ttttttttt ccccacccag cctcatttct gtttacaaaa
77941 gtataatcta ctaaattttt gtgagttata gttagcttaa gagaaagaga tttcttaaat
78001 ccagaaacta gaacattaaa gaaccagcag tactccaaaa aagctataaa attataatca
78061 attttcatca cttcattcag tgccatgtaa tcaattccag tcttgctgga tcttgggtta
78121 gcagtgtcac gaaccatcg attctctcaac cagacttctg gagatcttca ctgagtcaag
78181 tgtatggtct taaagttatt taagcaatat catcagaagc ctacaaccag agtacctgtc
78241 ataggctttt tcgtgagtct cagagcgagt cctgtgttgg agacaaacat tctgacctgt
78301 agctgattgc aggagctttc aggaaagtat caggggagaa tagtatctaa atgccaaaga
78361 gtatgaaatg gctgtgatga aaggtcagat gagagttcat tataccacaa ctgacaagga
78421 tattcgattt ttttggtggc atacaacgtt taaaataata attgaaatta tgactcaaaa
78481 cagtatacog gcacatagca tggataagga ggacattgac aaatttccag taatttttata
78541 caatttctga aaacataaca ttttatccat acaaatataa cccagggaag gttaggtatc
78601 tctttttatt ttatattttg tatggttttt cttataaaaa atacatccta ctttacctgc
78661 aaaacatgcc ctgcttttg catacttttc atagagttgc ttctagtttt taatacttag
78721 taatctctat tttccagaga aactaggaag aagacaattt taaactgtca tacattagca
78781 ttctatagta gattagaaaa tgtatgagta tacctatctcc caacatctag agggatgtgt
78841 ttcctcatta tacaatttct cagtgtggta gacaaaaata cgttattata cgggccaaaa
78901 tatctttact ctctctgtaa aaacaagaag ccaaaagtat ataaacttga attacttatg
78961 ttcagtaatt aatgttttag tatcgtatct tatttaaaat gatctagata ttgaatgcaa
79021 atctttttact tagcttaact ttaaggttaa aaattaccaa aagtatttta gaaactatta
79081 ttaggcagat ttactgtaaa aaattattat tgaaataatg cttttaataa gaatgacaat
79141 tagaatcaaa tctataagct ttaagatttt aaggatctag taagtataat attagcttat
79201 ttgagtagaa ctcaagcaga atagaaattt gttttatatt taatagtgat aactctgaag
79261 acatagttgt tttattacac caaaaatata aaattactct tatttaacta agttttatcg
79321 aaattgtgtt aacttgaaaa acatttggat cagttcctat atttattgga gtttggggaa
79381 tatttattta taaatgcttg gttttttttc caagccaagt tagaatagag cacttttaga
79441 agattttata agtgaatttt gcaatgctct ctggagtgaa gaaaaatcac atatacataa
79501 catacattaa tatacatata aacacaaata gaggtctcat agcttctatc ctgaaatatt
79561 agccatgaat caggcataaa tattctgatg gttaatttta gacatctgct tgattgatta
79621 agagatacta acatagctgg aaaagcacaa tttctgggca caagtgtgag ggtgtttctg
79681 caagacactg agataaggaa gatccaccct gacccaatgt agatagggcac tgatatggtt
79741 tggctgtgtc cccacccaaa tctcatcttg aattgtagtt cctacataatcc ctacatgttg
79801 agggatggac cctgtggtag gtgattgaat catggtggtg gttactgcca tgctgttctc

79861 atgatagtga gtgagctctg atgctctgat ggttctacaa ggggcttttc ccctttgct
79921 cagcacttct ccttacagct gccatgtgaa gaaggactct ttgcttcctc ttttgccatg
79981 attgtgaggc ccctccagcc atatggaact gccagcccat taaacctctt tgttcttttt
80041 tttttttttt tttttttttt tttttttga gatggagtct ggctctgtct cccaggctgg
80101 agtgcagtgg cgtgatcttg gctcactgca agctctgcct cctgggttca cgccattctc
80161 ctgcctcagc ctcccgagta gctgggacta caggtgcctg ccaccacccc tggctaattt
80221 tttgtatttt ttgtagagac ggggtttcac tgtgttagcc aggatggtct caatctcctg
80281 acctcatgat cctcccgcct tagcctccca aagtgctggg attacaggcc tgagccactg
80341 tgcccagccc aaacctcttt tttctttata aattgctcag actcaggtat tttttcatag
80401 cagtataaaa gtggactaat acaggcacca tccaattgat tgagagccca gatagaacaa
80461 caaggaagag gaaaggtgaa ttatctcctt ctgaaactga aatatccttc ctcccctgcc
80521 cttgacatcg gagctttaga gttacaccat tggcttccct gattctgagt cctttggaca
80581 tggactgagc catgctacca gctttccctg ttctccaact tggagacagc ctatcgtgga
80641 acttctcagc ctccataatt atgtcaacca attcccctaa tgagtcttct ctcatctatc
80701 tatctacata tatcctattg attctgcctt tctggagaac cctaatgtgg ttacaataac
80761 acaaaattca ctagtttata tggaagactt agtttttgcc tttgccccat tttatatttg
80821 tattataact gtttctggaa aatggaacaa gttttcgtct tcttcatatg agggctaaag
80881 ctttttttctc actaatattt ttggagattt ttaagatttt cttttgtctt gacatacaat
80941 cttatgaagg ctgagaatta aaattatttt tctattttat ttttcaggct caagtgtttg
81001 cttttgtaga ttcttgagca cgttgagagc ctccaaggct tggagggggg tgcctaaagt
81061 ttcagtgatt atagggagtt gagagactca actgggaaag gaaacgtcta aacagaggca
81121 atttgagaga taaaagtttt ctcaaaggag ccattaaagt tctaaataat tcttagtaaa
81181 gtcatgcaaa caggaaagga agtagacagg attagttcct tattggtgga acacatagtc
81241 agcggaggtt tgggaaggga gattttagtc aactgagaag ttcccatgaa aggagcaaga
81301 tcaagatctg atggaagggg aagagacacc atgaaacaaa atccaggaat aagttccaac
81361 ccaagaggag aacagagagg cctcaaaacc aaagctagga taagaaactt ctagcctgag
81421 agttaccttc tagacaaaga agactgagat tccaacccag cttcagagag tactcacatt
81481 ttgatgttac tcaaacttta ggctttttaa tgacttagcc atgcatgcaa aggcattcc
81541 ctaaggtggc acagaagacg gagcccctat atccaaagat agccaaggag aaagaaagac
81601 ccctgttgcc agagccagtg gataaaggca acagaaaaag agacaagggt ccttatgtga
81661 tgagaccttt tcagatttag gcttatataa actcctgaga actgggagga tgagagccac
81721 agatggggta ccaacatttc tactcatttg attacaagtt ctcgggcatc caaaatgatt
81781 aacaaaatga caatttctag ggcttctgtg ggatagtatg gaaggtcttt ttgaacgttt
81841 taatgctgtc aactgaagag tgatgaagtt catatatttg gaaaggaaag atttctttat
81901 ttttatgttt ctttattctt tttttttgag acggagtttt actcttgttg cccaggctgg
81961 agtgcaatgg catgatcttg gctcactgca acctccacct cccaggttca agtgactctc
82021 ctgcctcagc ctcccaatta gctgagatta tagatgcata ccaccatgcc cagctaattt
82081 tttgtacttc tagtagagac agggtttcac catgttggcc aggctggtct ccaactcctg
82141 ctgttagatg atccacccac ctcagcatcc caaagtgctg ggagtacagg catgagccac
82201 tgcgtccaat gagagattta tttcctataa agggttacag cctgcagggt agttcttctg
82261 acaggctagg aagtatagcc tccagccaga agccagaaac agacattttc aaatgtgagt
82321 taaaggaaac agtaatttat gctgagtggc atggccaaat acacatattt aataagctct
82381 aggaggagtc atgaatattt atgaaaggag aaatgcgtgc atgcgcaatt gagtgtcttg
82441 ctccttcatg ggtcccatgt acaaaaattg gcagtgttag catgatccca ggatggagtt
82501 ttcagccccc taacactaaa aggtgaagca gaggacatga aaactcactc tgtgcatcct
82561 ctgtacgctg gccagaacct ctccgtcatg ggtggtctct tatcaggcaa gaaaggagag
82621 gcggcttcag gcagttggtt gatatcagtg gtggagtctt tttcaagggc tggtttctgt
82681 taaatcctta gggaagaaag cctcatcatg gttagcaaag gagagggtat aacaaggtgt
82741 atctgactcc catcatccca tgctggccaa gctgagaact cagttttgaa agttactctt
82801 gggtcccctc agccaagagt gggtctgttc agtcagttgg gagcttagga tttcattttc
82861 atttatcatt gctaatggga aagggtacgc tgtctccatg gcagctgaat tcgcaagaaa
82921 ctccttggat ggggttaatg gcagYtgtat ttttctgKga SctYKgcttt aattggataa
82981 agtaagttct ggtaagattt cttccNttat cttcagtatc tcaaRtgttt tcaYttaaat
83041 aatctttata acaacttttg atgtctgagt ggaKtcccac acagtcatct attgtaagac
83101 tttctgattc cttttttttc ctttggtcat tMtgaatagg gcttctgtaa ataaYtgcat
83161 ggtagctttt gWtKggaaat aacatcaaag tagttgtcaa aatacYtagg aatgtKattt
83221 ttggattgta aggKgagact tgtttagctt tRgaaaaaaM tgMccaactt gtaatgggga
83281 ggaaaaaaat tttctNtgtt tttggaattc ttagatggRa cScKctgtaa aaactgacag
83341 attaaaatga gaaaaaSaga aaagtttaaa aacaYgtata YcttatggWt acatgggaga
83401 tactcaggga aaaatgagta aatctccaac aggtggcttt caRttcaagc ataaatacta
83461 tcttcaactt aaagaaagaa gatttgaggt gcagtggtNa gtggggagtt aaccagcaaa
83521 agcacattag acaagggtaa ggttYgttat acagacttaa gtccaYgcat tctccattga
83581 taagactctt Yagtgattta gttatccttc tcttcttgKt gtcgagagag gtagctttta
83641 aatggtgatt tcctttatag atgtaaattt tccttacaca agtgtaactt ctactctRtt

```
83701  ttcacaactt cgttagcatt ttttttttt tcaaaataat cagcttggaa taattcttaa
83761  gccaaagggа catattttgK ggtKgcatat tctggtttcc taccattata ttttggggtg
83821  gcatаKtttg gYcttataca ctgtgttcca cYggcaatga aaagagttct tgttttttcct
83881  ccagcaattt gtcatttgt agtttagcag ttctaagagc tatacaccag ctgtgctatc
83941  tcactgtggt tttcggttct ctagtatgtt gagcatcttt ttgtatgttt acttgccatc
84001  tgtagatctt ctttggtgag gttctgttca gatctgtgtg cattttcaat tgggttgttt
84061  aacttattgt ttagttttaa gatttttttа tatattttga atacaaattc tttctcagat
84121  ctgtatttttg caaatatttt cttcaatatg tggcttgtct ttttgttctc ttaacaaggt
84181  ctcttccaga gtataaactt taaatattaa gaaatccaca ttgtcatttc ttctgtgtat
84241  atcaaccttt tgtgtcattt gttaaaattc attaccaaac ccaaaggcac atagctttcc
84301  ttctatagtt tcttctagaa atggtacagt tttgcatttt tagtgtaagg atgattttga
84361  gtgattattt gtgtaagttg taaagttttc atctacacac atatcatttc ttatggtttc
84421  caattaactg ttccctatтt ctgggaaaga cacaggatag tgggctctgt tagagtagat
84481  agatagctag acatgaacag gaggggggaag ctcctggaaa agtgggaagtc tgggaagcct
84541  cacctggagg taccaccaaa aattcacata ttagtagcat ctctagtgct ggagtggatg
84601  ggcacttgtc aattgtgggt aggtgggaga agaggtacct atgcagaaag aaacacccta
84661  gaattcctct taagatgccc caatcatcat tcattctgca ataaaaatgt catacatcta
84721  ctctactgca cccagccctc ttctgcaatt tcaataatca attgtgctat ttgcctttct
84781  ttcagcaatg agattttatt tttctttcct aattatttca aacatgaact ttggttccag
84841  agaactagta tttccttgat ttataaattg agggcagctg ggcatggtgg ctcacgcctg
84901  taatcccagc actttgggag gccaaggcag gcagatcact gaaggtcagg ggatcaagac
84961  cagcctggca aacatggtga aaccccatct ccactaaaac tgcaaaaaat agccagccat
85021  ggtggcaggt gcctgtagtc ccagctactc agggagactga gcagagagaa tcgcttgaac
85081  ccgagaggtg gagactgtgg tgagccaagg tcgtgccact gcactctagc ctgggtaaca
85141  tagggagact ctatcctcaa aaaaaagata aaaaaattga gggtcatctc acagacgatc
85201  taataatgaa ttatttttt gtctttagaa aatcaacatt aacttttcta ctttttagata
85261  tcgtaactgc tgtgacttga aggacttatc tagaaaaagc cttaaaaaac tacggtcagc
85321  actgggtgaa tgggttgggg gaaccccacat aaaatcccca agacacctgg gagtccatgt
85381  ccccatgagt gggactgcag gcagctgtag cagactggat gggagagggc agcaggcagg
85441  agaactcggg gtctggagtc cacggttcta aggccaggga aaaccactgg caaagtgaaa
85501  tgcggagctt gacaggatga aatttgtgat tgtaaatgaa tatttgccat ttccaagtga
85561  gatcgccagt ggtggtggga tggatgggtg cccctccaag tgggctgcag tgaggagagc
85621  gtggcaccag gccaggatgc tcctgccagg aacacaggat ctgcacacgt ttaggaggaa
85681  acgctgggca gacccagctt ggagtcatct ctgctcttta catctgttaa gcctgtgaaa
85741  actgagagtc ggccggatgc agtggctcac gcctgtaatc ccagcacttt gggatgccga
85801  ggcgaatgga tcacctgagg tcaggagttc aagactagcc tggccaacat ggtgaaaccc
85861  catctctact aaaaatacag aaaattagcc gggtgtggtg gtaggtgcct gtaatcacag
85921  ctaatcggga agctgacaca gaagaatatc ttgaacatgg gaggcagagg ttgcaatgag
85981  cagagatggc gccattgcac tccagcctgg gtcacagagg gagactccgt caaaaaaaaa
86041  caaaaacaaa aacagaaaac tgagtctcag gaacagttcc cgagaaggaa aattgggccc
86101  gcatggaaat agacatttttt ctcccaccta gggcagggag tgaagtgaaa taggtctgtg
86161  gagtggactt tcacatagaa accatgtatt tcctaaattg ggggttattt ggggatcacc
86221  tggaggagta ttcctggttt tggtgaaaca cacgggggta tttttgtga agctgcaaat
86281  ctggcacagc aataacRgct ggggaactgg agatMaagga gaaggcatac taagtgctgt
86341  tgcaagtttc ccagaagtat gacattattg ggaagtaaac tacttttaa aacaaccgtg
86401  gcaataccac gtcagtaagS cagagacaac accatgaagt ttcatgacag aggccaaatS
86461  cagcccaaac ccagccagc agaggctgtc aactcagcgc cccagcgaga gccggaaggt
86521  tccacccctca gagtgcaga ccctctcgtg tgggctgcaa aggccatgtc tgcatccgg
86581  gcggtatgta cgctctgaga gatacatgcg tgttccgggg gttatatgag tgtgacgggt
86641  gtggcgtgag tctgactgtg tcacgggcgt tccaggggtt acgtgtgtgc tctgagggac
86701  acatgcgtgt tccRgggRtt atatgagtgt gacggStgta gcgttaggtg acRatgtcat
86761  ctccgMgttc caagcgttat gtgcgcactg agggacacat ccacgttccc ggggttggat
86821  gtggaaggca gctaccccga cgggtgtgct ctctgcatac gacgggtgct aacactagca
86881  tcacagatgc agtgttatta gtactacgga ggttattatc agtgtggcgg gtgttctaat
86941  tgctttcctg acgctacatt tctgttccaa gaccgcagct tggccctgtg gctgcctcgc
87001  cttggtgtg gagaatgaac ctcgagtgcg ctggattcac aggggatttt ggtttctaat
87061  tttccacatg aagggccaag gcgggtggat cacttgagat caggagttca agaccagctt
87121  gggcaaatag caagcccttt gtgtctacaa aaaaaaaaaa aaaaaaaaat tagatggcat
87181  gcttgcacgt acctgtagtc ccagctaccc aggaggctga agtgggagga ttgcttgagt
87241  ccagaagttt gaggctgcaa tgagccagcc atgatcgcac cactgcactc cagcctgggc
87301  gacagagtga gaccctgtct ctctctctct ctctctctct gtcacacaca
87361  cacacacaca cgttaaattt gttggattat atatttaggg ggttgagcac ttttggttat
87421  aaaatattta tgattgtggg aacaagttaa taaagacacg aaacttattt aaatgtccca
87481  gaacttttaag aacaaaaagc attcttagtt taaaaataag ttttacttta aaggtaatag
```

```
87541   tacacacata aattgttgtt aaaatcgaca gtaacaaaga gaagtaacaa tactaatggc
87601   ctgtcacaaa ctgattctta ataacctata taaacaaacg ttaagcccgg gcgctgggtg
87661   gctcatgcct gttatcccag cactttggga agccgaggca ggcagatcac ttgaggccag
87721   gagttccaga ccagcctgac caacatggtg aagcccaqtc tctaccaaaa atacaaaaaa
87781   attagccggg tatattggca tgcacctgta atcccagcta cttgggaggc tgaggcagga
87841   gaatccttga acccaggaag cagaggtcgc agtgagccga gatcatgcca ttgtgacagg
87901   agagaaactc tgtctcaaaa aaaaaattat atgtttacaa caggtgcatt cctcctcttg
87961   ctttctgagg acgccctgct atgtagctga gtagtcgcta ataaactatc ttaacttcac
88021   tatactctgt gacttgccaa aaggtctttc ccatgtgaaa tccaaaaacc tattcttggg
88081   gtctaggaca agacccattt tataatgaca aaactataca aattctagag gaaaacatgg
88141   aaagaaagct atgtgacctt gSgtttgqcc atgaqtttta acacgacact atcagaggca
88201   tttgaacccc tcctctaYat gaactccagg gtggtttatg ttccaYtggc taagRgaaag
88261   ttttcttcaa aaatgtgaca tgatttgagg tcaaacatta atatcaagKW aactcaaaag
88321   attgagaagc tagcattagt tctgggaaaa ccagaagtgt gccttttttt ggaaataatc
88381   attggtagca caaacttaag aatctccaaa ggaaataaaa atgagttatt aacttacagt
88441   tttcaccaat taagatataa atgaagctaa Ygaaatccgg aaatacaatt tcactgtttt
88501   taatgttcat taaaaaaaaa aaaaaaaacc ttatcaaata gccccagtaa gtcaccaatt
88561   aagtctttac tacttaaaag caaaatccac ctatgtcctg aacacttatc cactttacRa
88621   gcctcattat atgtactgga gacaaaattc agaaataaat aaatatatat gtacatatat
88681   acaaatatat ttcaaattaa aaaatacttt tagagagtgg tatgtattac atttagaaat
88741   taataacgaa gtaaattatg ggatgtcatc cacgcctgtc ccaaaggtac cgaatttata
88801   aatcatctca ggtgcggagc aggacaggtt gaaaatagga atgacatgaa cccgcgcgga
88861   acagctgccg gcgcggtgtc cagggcggca ccccgcccgg tccYggcccc tccagccctg
88921   ggcccgaccc ctactacgcc tctgcctcga cgcgaacgcg gaqcccgagc gcgcgtcacg
88981   ccgtgtgggg ccgaagaggc tgctacccag aggcggagtg cgggctcgcg agggtcccca
89041   cccSactctc gctccgccca gcacctacgg actcgcgtcc ccgccgcgcg ccgactcggg
89101   agcagcaccg cccccggcac aggagcctca cgcgcctctt acctaacagg aagttgggtg
89161   gaagcagcgc ggacccacgg cacaccgaac gcactccaac agaccccgac gcagacacgc
89221   gctttcaacc ggcggagaca ctggcaggtc aatagagata ttgactatat aaacaaaaga
89281   atgacaaatt aatagtgtaa tggataactt gactttggca aattagcttt gtactggtga
89341   aagtacaact aaaaggcaat gtcactccaa taatcaccag agtaatcaat ttgcttattg
89401   ctgtcccttt aaatatagtt ctctggtatc aactaacatg tttttaacta atgatgcttc
89461   ttaaagaaaa gggaaaagac ctttttcttt ctttcagtct tcaatgattc actgcttcat
89521   ctcgctccac caaagataaa tgaaatctac atctcttata cattaacaat gcatgacaat
89581   ttacaaatag ctaaattttt ggagctaact ttaagtacct gaatggaatt taatcaaccc
89641   actaatctcc ttctcacttc tcagttattt atcaagttta tgtcaaggga caaggaaaaa
89701   ttatccaaac attgtttaaa acaatcatca ttaattagta acactatcc aggggggttt
89761   ttaacctttc ccccactcaa ggattattct aatgtcagag tagaataaaa aataagtgca
89821   gcgatgctga ctcttccaag cttaacattt ctcacaagtc aattagcttt gtactggtgg
89881   gagggcgtga agggctgctt gcggtagttg tgtagcagca gcacaatggc cgcagacaag
89941   gaaaacagtt tctaaaaatt cctcgtatat aattttatat ttttgacaag attaatgacc
90001   catgctccct tcctctccat ttcttttttt ggaattctgt tggtatgtag ttactatatt
90061   ttattaaagg aaattagcct tatctctttt tatattttat taaagaaaat tattatatta
90121   ttcctttata tttttattaa aggattttat tattattaaa ggaaattagc cttatctctt
90181   attatatttt ttatgacctt caaagtagtg tctctgctta aaagtgtacc ctggccggcc
90241   gtggtggctc acacctgtaa ttccagcact ttgggaggcc gaggcgggtg gatcacgagg
90301   tcaggagatc gagaccatcc tggctaacac ggtgaaaccc cgtctgtact aaaaatacaa
90361   aaaattagcc gggcatagtg gcgggcgcct gtagtcccag ctactcagga ggctcaggca
90421   ggagaatggc gtgaacccgg gaqacggagc ttgcggtgag ctgagatcgc acgctgcac
90481   tccagcctgg gcgacagagc aagactccgt ctcaaaaaaa aaaaaaaaaa NgtRtaccct
90541   gaagcacaca tcaagcgaca tgtagagttc ataaattctg gccaaatggt catacctcaa
90601   acctcatcag caStaaggct ctttacttgc actgacaaat atgaacgctg gggaatttgg
90661   aaatgatata taatatataa tattatatat ataatagata tataatatat aatatatata
90721   atacatatat aatattatat atgtaataga tatacaatat ataatatata atagatatat
90781   aatattatat ataatagata tataatatta tatataatag atatataata tataactttc
90841   catgtgattt
```

ELP3 genomic sequence (SEQ ID NO: 2)

>8:27927301-28022150

1	gagaaaataa	ttcaaagttg	tatttaaatg	ttcagagggg	gaataatacc	aggatccttt
61	ctcaaaaaag	aaacacatgt	ctggaatagg	cagtgatgtg	ctgcagccag	ctcgtaccag
121	ctcctgaaag	ccaacagcac	acatcacttt	cctactctgc	attcagtgac	gtcacactgg
181	tagcttgaaa	ttgacaatgt	tgggactgtt	Ycagtcctga	atctcaaact	gataacccaa
241	atccataacc	acattgtgat	ccctaatctt	caaccaaata	attccagctg	acatgtgacc
301	acagcttatc	aatactaaga	ggcacatcat	ttccctgttt	aagatttctg	aaattgagat
361	gcatcttgca	actgctatag	accaggtgac	aatcacaagg	tggttgtcac	tgcctgcgtg
421	ttatgggctg	aaatgtatcc	ccctccaaaa	ttcaaatgtt	gaggtcccaa	tcYccactaa
481	ctcctattta	caccacagga	attggcaaat	ggtacacatc	agccttttgg	gttttttgtt
541	tgtttgtttg	ttttggggga	tttttttgtt	tttaaacaaa	gagctagttg	ttaaacattt
601	acaagcgcaa	cgcaacacaa	acctggctaa	ggtcctagaa	aagtgacagt	ttcttaagta
661	gttagtgagt	aatcatacac	attttaatgc	agactaatgt	tgaaacatta	gtctgggtgc
721	ggtggttcac	acctgtaatc	ctagcacttt	gggaggccaa	ggcaggcgga	tcacaaggtc
781	aggagttcga	gaccagcctg	gccaatatgg	tgaaacccca	tctctactaa	aaaatacaaa
841	aattagccag	gcatggtggt	gcgcacttgt	agtcgcagct	actcgggagg	ctgagacaag
901	agaattgttt	gaacccggga	ggtagaggtt	gcaatgagcc	aagatcatgc	cactgcactc
961	cagcctgggt	gacagagaga	ttccatctca	aaaaaaaaaa	aaaaaaaaag	tcaagcaatt
1021	aagaattatt	tgagggagtc	ttttttgtg	cttagaaaaa	cagtgtcgtg	gagaagtcat
1081	actagaatca	tatagaaata	gcattacata	ttctttcatt	cttcttactt	aaaaaaaaag
1141	agaaaaacat	tcacctatag	aatgtgcatg	tgcgtgtgtg	ggtatttgag	ggaggtagaa
1201	agcagtgaag	agttgtcaat	ctctttctga	tgcaaagata	taaagagctg	agtgagtaga
1261	cgccttgcag	tccactggga	ctggtgagaa	gccgtgtccc	tggcaagcta	taagcacgtg
1321	tagttaaggc	tggaatacgg	atatctgtgc	agactgccag	aagcccaccc	ccaccaaccc
1381	ccttatagag	tgagctgaag	ttgcaaaaag	aatctatctg	ctgagatttt	gctttgattg
1441	agttttcact	ctaggaaaaa	gtttagggaa	agctgaaact	attttctact	gggagatgaa
1501	attaatgtag	aattaagttt	aagtagagtt	ttaaaRcagt	tccaagaaag	gcatgtgctt
1561	agctgtgtcc	agatgtttgc	attatttaaa	atctggacct	aaatcttgta	taacttttct
1621	aaaaattact	gaagattagt	taacatttat	gctttttatt	gtagtaaaaa	gaaatgtttt
1681	tatagtgtca	gtgaagtgac	tctagtataa	aggttcata	ttattgtaaa	agagaagtag
1741	aaacagctac	agctagaggt	aggatccaag	atgttagtag	atattcatta	aattatgcaa
1801	cagaaacatt	acacactgtt	ctaatttaaa	cacatggctt	gtcataataa	aacgtaacac
1861	aatatattaa	agtttgtaaa	aagatgttgt	atgtgagaga	ggagaaaacg	tggaagctca
1921	aaccagaagg	gaggctaggt	gtggtggctc	acacctgtaa	tcccagcact	ttgggaagcc
1981	gaggcaggtg	gattgcctaa	gctcaggaat	tcaggaccag	cctagccaac	atggtgaaac
2041	cccgtctcta	ctaaaaatac	aaaaaattag	tcgggcatgg	aggcacacgc	ctgtagtccc
2101	aactactcgg	gaggctgaag	caggagaatt	ccttgagcct	gggaagcaga	ggctgcagtg
2161	agccatgatc	acgccattga	actccagcca	ggacaacaaa	ggaagacact	atcttaaaaa
2221	aattaaataa	aaggccgggc	acggtggctc	atgcctgtaa	tcccagcact	tcgggaggcc
2281	gaggcgggca	aatcaccgga	ggtctggagt	ttgagaccag	cctgatcaac	atggagaaac
2341	cccgtctcta	ctaaaaatac	aaaattagcc	aggcatggtg	gtgagtgcct	gtaatcccag
2401	ctactcggga	ggctgaggca	ggagaatcgc	ttgaaccagg	gaggcagata	ttgtggtaag
2461	ccaagatcgt	gccattacat	tccagcctgg	gcaacaagaa	caaaactctg	ttaaaaaaaa
2521	agaaaaaagg	aaaggaaaag	aaaggaaagg	aaaggaaagg	aagaaagaaa	acagaagggt
2581	tattcaatgg	aagcagaatc	agaaaggata	tagtaaagtt	ggagttacac	tgaaaccagt
2641	aatatcaatc	atgacccagc	tgggtgaggt	ggctcatgcc	tgtaatccta	gtactttggg
2701	aggctgagac	aggtgggtca	cctgaggtca	ggagttcgag	accagcctgg	ccaatatggt
2761	gaaaccctgt	cttcactaaa	actacaaaaa	ttagccagtt	gtggtggcgc	atgcctgtaa
2821	tcccagctac	ctgggagact	gaggcaggag	aatcacttga	acccaggagg	cagaggttgc
2881	agtgagccaa	cattgtgcca	ctgcattcta	gcctgggcaa	cagagccagg	ctccgtctca
2941	aaaaaaaaaa	aaaatcatga	cctgattttt	aaaaatctac	ctgaaatcag	tgacataaat
3001	catgactcat	tttttaaatc	cacctttttct	agctttgtca	tgaaaattat	gttgcagtga
3061	tgtcactctg	ccactgtctt	acttgtatga	aataatttga	tctgagcccc	tagcactctt
3121	tttttgctgt	tgttagagat	gggggtcttg	ctatgttgcc	ctagctggtc	ttgaactcct
3181	ggcctcatac	gatcctccca	cctcggcctc	ccaaagtgct	gagattacag	gtgtgagcca
3241	ctgctcctgg	cccaattatt	atttttaatg	ttattctcgc	taaaagaaac	cccagattcc
3301	tggggagtag	ttgttccata	tcttggggca	gggaaaaata	aagtgaacct	gaatatcttg
3361	ttgtagctag	acagcaagaa	tgttttttaa	atgctaaagg	gagtaatgct	aaagggagtc
3421	agcttaaagg	gttcccactg	gccaaaaagt	gacacattga	gcatcagaat	gaacacaata
3481	gttctgtgaa	aagctatgag	ctcattatga	tcctaaaact	gagtaaataa	aataaggtat
3541	gttaaagtaa	aggcattaac	cacctcaaac	aatatatgcc	tgagactgtc	aaaattcagt

```
3601  ctgtaaattc cacttgggca agtcctaaaa gtttacctaa catataaaag aatattaaca
3661  gtcttagtag gggcacaaaa atcctgtcag gtcaaatcag gcagtaaaac tttgtgaatt
3721  aggttaaaat aaaaagtcgt gtgacagttt atagtaaaaa ctgagccaag gcggccaggt
3781  gcattggctc atgcctgtaa tccagcact ttgagaggct gaggggagat caccgagagt
3841  cgggagtttg agaccagcct gaccagcatg gagaaacccc gtctctacta aaagtacaaa
3901  attagctggg cctggtggcc catgcctgta atcccagcta cttgggaggc tgaggcagga
3961  gaattgcttg aacccaggag gcggaggttg cggtgagcca agatagcgcc attgcactcc
4021  agcctgggca acaggagcga aacaaaacaa aacaaaacaa aaaacaaaca aaacaaaaca
4081  aaaaaaacca aactgggtca aggcaaaatt taagggaagg tcaagtgaac cataacatac
4141  caggtagtaa gaaaagatgt ggagctagaa agcctcgtta ctataggatg gggccccaat
4201  caggcatctt ggaaggatct atgtgcctgt gtctcagcct tgaatctcaa actagtaact
4261  caaatccata actacattgt gatccccaat cttcaaccac ttaacttcag ctgatatgtg
4321  actacagctt atcaatacta agaggcacat tgtttccccg tttaatattt ttgaaattga
4381  ggtgcatctt gcaactgctg caggccaggt ggcagtcaca aggtggttgt cactgcctgt
4441  gtgttatggg ctgaaatgta tcccccctca aaattcacat gttgaggtcc taatctccac
4501  tacctaaaaa tgtgaccttа tatggaaatt gggtcattga ggatgaaatg tattaagatg
4561  aagtcataat ggagtagggt gggccccтaa tccaatgact ggtgtcttta aaaaaagggg
4621  aaatttggat acagagacac acacatgagg agaatggcat atgaagactg gagttgtgct
4681  gccacaagcc aggaattacc agaagcaagc agacagaact gtaccagatc cttcctgcag
4741  tttcagaggg agcatggcgc tgctaatacc ttgatttttgg acttccagcc tccagaactg
4801  ggagataata attttctgtc gttccaagct acccagctgt ggtgcttagg aggttcatac
4861  actgcacatg ggtgaacttg gtcacagctg ttcacattgc ccttccttct aatgagttgt
4921  gtgcattact taactgccat ttaatatgtc ttttaaaaga ttatgttatg attcagcatt
4981  gaaaggtcag cattttccag gccgttacat cgaaaggcct ggaaatggaa acgtggggca
5041  tatacttgat gttagtggaa gtatggttgg tgtagacagt aattccagat ttttttgcaa
5101  agcaacacct aagtgcttca tgggacctag gaaagggaga catccacatg tagatgaagg
5161  tgggttgtgt tttgatactg aggtgtatgc aaagtgactg cctatcccac acccagccaa
5221  aaaaaaaagt gatggaaact caaagaatgc cttatаaaga acttctgtct catgttttct
5281  gtgattaaaa ctaaatttgc tccaaggcta ggcattgtgg ctcacacctg taatcccagt
5341  gctttgggag gcccaagcag gagaattgct tgagcccagg aattagagac cagcctgggc
5401  aacataccct gtctctacaa aaaatttaaa aattagctgg atgtggtggt gcatacggt
5461  ataccggtag tcctagctcc ttgggaggct ggtggtggtc aggggtgcg gagtgcgggc
5521  aggaagatag cttgagccca ggaattcaac gttgcagtga gttatcattg tgccactaca
5581  ctccagcctg gctaacagag tgagacccat ctgggaaaaa aaaaaagttc caaacaacRg
5641  catgtagtac aagtaaaggt ttcacaataa ttcaaactga aataaagtgg ttggagaatg
5701  aaggcatcac cttgccatca gaggtgtggg ttttaggcct cagaagaact tgcaccatag
5761  cggtgacagc ttgaaacctc ctgcaaactg atgttatgct gcccaggccc taactcatac
5821  aaaccaattc ggcatgttta ctggcatagt tgtaaattgt gtattgaagt attctacgtt
5881  tccatttcca gggataatat gatcaggcac tcatacaatg catatttatt taatacccaac
5941  aagaacaatt caacagacca agaccagctg tactaagttt tgcctcgtta aaactggcat
6001  tcaagaattg cctgatagaa tattttggct taagtatgag gcctaatgat attgcgctag
6061  aaacaaaagc tttgaaattt tcaattccac gttgcacaac agacattttc tgtatcaata
6121  ttattgaagg caaaatacag aaagaaattg aatatagagc tggtcatcgg ccaaatgttt
6181  ttactattga atccaatacc gaagattttg tttcagccaa acatatcatc tgtcacatgg
6241  tacttactct gatatatccc ttatgttgtg ttgtttatat ttatcttaa acttggtttt
6301  agttttatag ttgtacaaga ctattatagg ccagacgtgg tggctcacgt tggtaatccc
6361  agcactttgg gaggccgagg tgggtagatc accagaggtc aggagttcga gaccagccctg
6421  gctaacatgg tgaaacctca tctctactaa aaatacaaaa attagctggg catagtggca
6481  ggcacttgta atcccagcta cttgggaggc tgaggcagga aaatcgtttg aacccagggg
6541  tcagaggttg cagtgagccg agattgcacc actgcactcc agcctgggca acggagcgca
6601  actctgtctc aaaataaaaa agttaaaaaa aaagactata ataataataa gttgtatgtt
6661  tgtacctact ttagtgataa aatagtaaaa ataggagaac actaagtgca gctcaggcct
6721  tatccctgtc cactccctct cacactctcc ctctgagcct ttccaagcta cttgcctgtc
6781  attcgccaaa cacagcagcc tgtgtgaacg gtgttcttgc ttctgcctca aaagtgcctt
6841  ctcgactttt tcaccttact aaagactaca gcttctttaa aattctgctc tgcagagcac
6901  tgtggtgctt gccgagctgt agtcccagct acgtgggagg ctgaggcagg aggatcactt
6961  cagcccaaga gtttgagacc agcctgggca acatagtgga aaccccatct ttaaaaataa
7021  taataataaa attggccagg tgcagtggct catgcctgta atcccagcat tttggagggc
7081  caaggcaggc agatcacctg aggtcaggag ttcaagacca gcctagtcaa catggtaaaa
7141  ccctgtctct actaaaaata caaaaaatta gccaggcatgg tgaccagccct ggtcaacatg
7201  gtaaaaccct ctctctacta aaaatacaaa aattaaccag gcatggtggc atgcacctgt
7261  aatcccagct actcaggagg ctgaggcagg ataatcactt gaacccagga gacggaggtt
7321  gcagtgagcc gagtttgtcc cactgcactc cagcctgggt gacaaagtga gactaagtct
7381  caaaaaataa taataataaa ataaaattct gctcagaggc tgagttttcc ttgaacacct
```

```
7441    ccccagtccc acctctcctg ccaccagtgt gacctggcat ctttcctccg tgtcccatag
7501    cactcaacaa ttcctccact gtatggagag cccagactca cctgggccta ctcctctgtg
7561    gaccacatgc tcattcgacc ctctccaacaa tcacgggaga tagatatcat tatctccctg
7621    ctttaagagt gagaaaatgg tgcctcagag aggtaactga agcagtagga ctgagttaaa
7681    tccaaactgt ctcctatagg tcagtaatcc cagcactttg ggaggtcaag gcaggtggat
7741    cacttgagcc caggagtttg agaacagtct ggacaacatg gtgcaatccc atctctacaa
7801    aaaatacaaa aattagccag acatggcggt gcatgcctat agtcccagct acttgagagg
7861    ctgaggtggg aggatctctt gagcctggga ggcagaggtt gcagtgagtc aagatcacac
7921    cgctgcactt cagcctggcc aacagagtga gacccgcgtc tcaaaacaaa agaaactaac
7981    tgtctattcc aaaacttgg ccctgcaac tacacaatac caggcataca tttgtctccc
8041    aaaatctagt tgctgggata cagaaaaaca catagagaaa cctattaact caccttcagt
8101    ttttccttga gaattctagt cctttgtagt tttatcattt catttctttc taaaacagcc
8161    tctcgctgac tctgaatagc ttgctaggtt gtgaaaggaa atagaagcat gcagagagta
8221    gcgttatcaa cagtgatgag gtggcaagat gcacatttta ttggcagatt ttcatttggt
8281    ccaaacagtc aaatatgcat gcactgtatt agaattatac acagttgccg ggcacggtgg
8341    ctcatgcctg taatcctagc ccgttgggag gccaaggtag gcagatcaca agctcaagag
8401    atcgagacca tcctggctaa tccagtgaaa ccccatctct actaagaata caaaaaatta
8461    gctaggcgtg gcggcacgtg cctgtagtcc cagctactcg ggaggctgag gcaggagaat
8521    tgcttgaaca caggaagcag agcttgcagt gagtcgagat cgcgccactg cactccagcc
8581    tgggcgacag agtgagactg tatctcaaaa aaaaaaaaaa aatacacagt tgacccttgg
8641    actacatggg tttgaactgc gtaggtccac ttatacgtgg attcttttttc aataattgaa
8701    aaagatttga agatttgcaa caatctgaaa aaactcacag acaaaccctg tagcctagaa
8761    gtatcaaaaa attaacaaaa aggtgtcatg aatacataaa atagatgtag atcccagttt
8821    atatttgata atgtactacc acgaaatgca cacgattcta tcatgaaaag ttaaaattta
8881    tcaaaacttc tgtaaacatc tatagactac atggccaccat tgcgcagtcaa gaggaatgta
8941    aacaaacatt aagatgcagt attaaatcat aactgcataa aattaactgt agtacatact
9001    atactactgt aataacttca gagccacctc ctgttgctgg tgtggtgagc tcaagtgttg
9061    caaatatcca cttaaagcgc caaacaccat gtgatactaa tgatctccat gtgaacaact
9121    gctccagtaa attgcgtatg gcaataaaaa gtgagctctt gcagtttcta tgtatttttc
9181    agcctgttta gagcaatacc ctaaatcttg aataacacca tcggacccat gtgaagtcca
9241    gtgatcctgg aggggctccc aagtagcaga gaaaagtcat gacattacaa gaaaaagttg
9301    aatcgcttca tatgtgccgt agattgaggt ctgcagctgc tgttgcctgt catttcagat
9361    gtacgattca tcttgtaaac agatgaagta aacttatgct attgataaat acggtgccgt
9421    attgtaaatg tattttctct tccttatgat tttctttcct ttttttttct ttttttgtt
9481    gttgttgttt gagatggagt ctcactgttg ctcaggctgg agtgcagtgg cgcgatctcg
9541    gctcagtgca acctccgcct ccaggttca agtgactctc ctgcctcagc ctactgagta
9601    gctgggatta caggtccatt ccaccaggcc cagctaattt ttgcgttttt agtagaaacg
9661    gggtttcacc atgttggttg ggctggtctt aactcctgac ctcgtgatcc gcccacctca
9721    gccttccaaa gtgctgggat tacaggcatg agtcaccaag tcctgccatg attttcttaa
9781    tgacattttc ttttctctag cttacttatt ttaagaatac agaacataat acatacacaa
9841    aatatgtatt aatcgactgt ttatgctatc ggtaagactg ccaatcaaca gtggctatta
9901    gtagttaagt ttttggggaa tcaaaaatta tgtgtggatt ttcaattgag cagggagttg
9961    gcacactaat ctctacattg ttcaagagcc aactgtaata tcagtcataa aaagtattat
10021   ttaaaaagaa ttagttcagg ccgggcgcgg tggctcacgc ctgtaatccc agcactttgg
10081   gaggctgaag ccggtggatc acctgaggtc aggggttcaa gaccagcctg gccaacgtgg
10141   tgaaacccca tctctactaa aaatacaaaa attagccagg catgatggtg ggtacctgta
10201   atcccagcta ctctgggagg tgaattagga gaattgcttg aacctgggag gcagaggttg
10261   ccgtgagccg agatcgccgc aatgcactcc agcctgggtg acagagcgag actctgtctc
10321   aaaaaaataa aaaataaata gataataatt taaaaataaa aatgaaaaaa actagttcat
10381   acttacattt cctgcctttc tttccctgaa atgaaattag aaaaatgtaa caattactta
10441   atttttacta tgtgtcactg cagtctttcg actttcccca aaagcagcac acactccctg
10501   tgtctgtgcc ttttcataag ttctttcttt gacccaatgc tctctcttct gacccatctc
10561   cagcatccac ttgaaaaaag tgccttcatt tctcaacggc cagccagcgt tttgtcagct
10621   gtgaacattt tctgtgacct cactccctgt cccagtcaaa aatgcagccc tctccacctg
10681   ggttcccata gcacctggct tgtcccttca tgtataactt ttaaccctct tttagatggt
10741   gagctcaaag actgggcaat gtgcctctga atccacagcc cctacctatg ttcaataaat
10801   gcttatcatt aataaattag atttaattat gttaattttt ttttttttg agacggagtc
10861   tcactctgtt gcccaggctg gagtgcagtg gtacgatctc agctcactgc aacctccaca
10921   ttccaggttc aagcgattcc cctgcctcag cctcctgagt agctgggact acaggtgtgc
10981   atcaccacgc ccggccaatt tattttgtat ttttagtac agatggggtt caccatgttg
11041   gccaggatgg tctcaatctc ctgacctttgt gatctgcccg cctcagcctc ccaaagtgct
11101   gggattacag gtgtgagcca ccacactcag cctaattgtg ttaatttag tgttggcatt
11161   ggaaaggaag ggctggagat attctctgct ggggtgagat ggggagaaat gcaggagaga
11221   aaaaatgaag ctgcaattcc aacccagacc atgacagcaa gggaattcct ggagacagca
```

```
11281  gtcagaccta agcttcagtg ggtgtggagg aaatggtgga ggggctgtaa aggagctctt
11341  gttggaggtg agacgcatcc gtgacatcac atccgtgag cacacacccc atggatccag
11401  gaaagcccag tttatacccg ctgatcccct ctaaggacta atcatacccc ctctcactct
11461  caaaatttgtc ccaatataga aggttagtta tagtcttcct aactatagg acaacagagc
11521  tctccataga aatcaacatc tattaagccc aaaaatgcat acctttcatt gtaatttgtt
11581  ataatacaac tcttagagaa tgcatctacc ttctcccgaa gttctaaac ttttgaggac
11641  ctgttccaag tgagttaaaa agttcaggag tctctggctg gggatgctgg gcttgatacc
11701  taggtgatgg gttgatctgt gcatctaacc accatggcac atgttaccct gtgtaacaaa
11761  cctgcacatc ctgcacatgt accctggaac ttaaaataaa aataaaaatt taatgatttt
11821  taaaaagctc aggagtacaa aaacctgaaa catcaaagct gtaccctggg ctgggtgcag
11881  tggctcacac ctgtaatccc agcactttgg gaggccaagg cgggcagatc acctgaggtc
11941  cggagttcaa gaccaccccg gccaacatgg cgaaacccca tctctactaa aatacaaaaa
12001  ttagctgggt ggaccggccg gcgcctgtaa tcccagccac tcgggaggct gaggcaggag
12061  aattgctttga acaaggaga cggaggttgc agtgagctga gatcgtgcca ttgcactcca
12121  gcctgggcgg cacagcaaga ctctgtgcca aaaaaaaaaa agctgtaccc taccagatag
12181  gattataggc tgtacccct agttatgggg gcatctacac tttctacatc tgtggagcag
12241  gtgggatcat cacatcacac agtgcaggag gtacaccatc tgcatctggt acatgtgagt
12301  ggcaccccca gagctgtgta ggggacacca gcttggcact aagcagctac cctggaaggt
12361  tcagattcct aagacaaccc aaccaagggt cctgatgtcc caggaagtca cccagcctt
12421  tctttcctcc ccaacaatca cttcctgaag ccctctaacc acgttacaaa gtcaagctcc
12481  atgctactgt agtcaggacc cacagaggaa agcccctgac tggagcccac atccttgcaa
12541  gcccagcaca ataccttagg tattctggca agtggagttt gtccatcttg gtgaccacca
12601  gggccacgtc cctacagaag ccccgctggc aggctttgat gctctcattc agaaggtctt
12661  cgtgggcttg cccccagaa actcgctcta tgtcgctgat cacccagatc actgagcact
12721  tgtcaatggt ctgcaaaaca tgaccacggc atgtgtcagc acaggaatgg agtcacagtt
12781  cctgaggacc ggttcctaa tgtatccctt aagcctctcc ctcagtccc acccctcacc
12841  gctccccacc gcactctgtg cactagctgg actgagctat gagtcatttc tcatatgtgc
12901  cttgttctgt taattccctg gccacagcct ctgcctagcc cccatttgtt cctcaagact
12961  gtggaggacc tctcgggcat tgggctggcc tctgcatcct gtaacacctg gacttacctc
13021  aagcagcgcc tctgagacac agtgactgca ccaggtctgc tctctgcccc ttgatgggaa
13081  gcgactgtct gcacctttcc tcttgggatc cacctcacct caagcccagt gcttggcaca
13141  caggagaggc ttcacagaag tttgtggcat tagagattga cagaattccc taaatcagtc
13201  ctccagtccc agtcccagat ccatcactgg cttgctttat ctcagttgtc ccctggggaa
13261  aattcttgtt tttccagaac taggtttggt ggtgcaccta ccctcaagct gtcacctgac
13321  ggcagcattt tgatgtttga ctgcccctgc acgtttagtt caatgccacc agatggcagc
13381  atggagccag aaaccatatg acaagttgca aaggccaatg aacatgaaac aacatatatg
13441  catgaatgtt gctttattaa atatgcaact ttcacatgac gatcatgtgt agcctgtgga
13501  catttctcta attgtattgt tactcttgtc ttacctccac ataaatgaaa atctggttca
13561  actcaggat tgagtttatt tgtggttcct cagtgctttg catacaaagg gatgacaagt
13621  ttgtgacttg aaaattaaat catcattttg ctttatacca gtagtttttа actagtagag
13681  gttttgtgcc ccagaaaata taaacagtct ccaatttgtg atgatttcagc ttacaatttt
13741  tcttttcgac tttacaatgg gtttactgaa caattggtaa gtccagtaca atcgggggcta
13801  atgatggtta tgatttcagc ttacagtggg cttatcagga tgcaattcta tggtacatca
13861  atgagcatct gtatttggca aaaaatgtct ggagacattt ttaattgtga caaccttggg
13921  ggggtacttg aaggtaaagg ccgaggatgc agctaaacat tcttcaatgc ccaggacagc
13981  ccaaccccag ctcccatccc acaaataatt atctgacagc ccaaaatgtc aagagtttga
14041  gaaaccctga tccagggcag tgggtttcag cttgctttta gcatgggagg ctcttttcaaa
14101  tgaaatctta gttagatttc caacatataa acttgatttt taaaaagcag aactgctctg
14161  gttgaattgg gagtgcagga cccagaacca ccatcggctc aatgccctct accctctgtc
14221  caggaacctt ttggctccat acatcactgc ttaaaaagca tctgcttctc aagttagaga
14281  aacccctttgg attatagggа agtaatgaag cccaagcggt aaagagactc aagtagggcc
14341  acacgacgat ggatcctgtc tctcctctat aagtgaatgg actttgattt aggcaagaaa
14401  ataaaaacca ttacagccct tctgctgccc aaactatаat caacttagaa aagctttggg
14461  ctctgggcca gatgtggtgg ctcacgcctg taatcccaac attttgggag gctaaagcag
14521  gcagatcact tgagctcagg agttcaccag cctgggcaat atggtaaaat ctcatctcta
14581  caaaaaaaaa aaaaaattag ccaagtgtgg ttgtgtgcac ctgtagcccc agctactcgg
14641  gaggctggga cagcaggatt gctcaagccc aggaggtcga ggttgcagtc agccatgatt
14701  atgccactgt actccagtcc aggcaacaga gcaagatgct gtagcaaaca aaacaaaaca
14761  aaagtagaag cagcttccag ctctgtagtg tcaacagtgg gcagagaatg gtccagccag
14821  cggaaggcca taagtatgcc aggctgggtg ctccttaagg gcagggccc cgtcaccttc
14881  atattcccca tggtcctggt aagccacagg tgcttagtgt ttactaacat gagaaaagga
14941  cagcaaccat aaagggtgca gtggttaaat ttcagaccga ccccacacaa agctcccact
15001  gccaggggttt ggtaaagtta gtgtcgcaga agatacaaaa aagcatttcg ataaaacctg
15061  aactgccaga cttaggagta gatgaggtgg caccccacca ccccaaact gcatctccc
```

15121 aggccccgc tatgagaatg ggacttagag gagttcagag acatgcctca agtcacgtga
15181 cttctaagtg gcagatcaga ttcagggaca tctgaattca taacgggttt tagggaaggc
15241 aagactggca gcctgagaga catagggagg gcaactgtgt cgttctccct gcagaggggg
15301 gtcttgagta acttcttgtg agaggaggtc aagaaaaccc acaagaatgc aggggagctg
15361 ggccaggcag agcacggtgg gaaccatccc tcgcttcagc ctgacctcct cagagcacat
15421 tttctgagcc agatctgccg tctttgataa gctgcccagt gtatctgaac tggctgcagc
15481 cgcggctcca tccagcgaga ggccctggca gccttcctgg gctgtcgctc tctcggccgg
15541 gcctggaact agccaagatt cgcgatttcc accccaggat ccgaggtctt gcagaaacta
15601 aggctcacaa ggccaggcct gagccaccga ccaaggggaa ggacacagag actgccttcc
15661 tcctgcagga ggtggataat atagagcgtg ccctggggga ggtggggtag atagagcccc
15721 agcagggaag ttaggaaacc tgctctccaa ggctgtgtgg tcctggacaa gtgactttcc
15781 ctctctgagc cttcatgtct tcatctgtac aatcagggca gaggctagag cttgctctag
15841 attgtgactg gaagtcgtgg ttaccaagct cccctggcac aatcattcat ctaaacaaac
15901 ctgtggagtt taaagaactg gattctttgg cagctgctgt gctgctcaca actcactgat
15961 gctggtcccc ctctcccagt ccccttccag ctcctgggct cctgtgttcc tcccaccctg
16021 tgctccagag cgcctctgtt taccgcgccc tttctcaatc acatgcccca gtccctctct
16081 tcctgcaagt tttcccagga agccaaactc tggagcagta gtactaaaga ccccagaact
16141 tttccaggca tgtcttccat agtctccctc ctccacggac cccatgctcc ttctcccatt
16201 cacccaggaa gattcaccct gcccccacca cgccagcttc ctcagacctc cagctctatg
16261 ctgatgctgc ttacagccaa cacagttgca gcctcttggt tcttggtgac tggctgcagc
16321 ttctctgctt tgtccccaac acttggcctc ccagttccct tctgtccttg gtcactctgt
16381 ttcctcttaa gccactctat tgctggtctt tctcatacat cacacacact tgtcccagct
16441 ccaatagtca catcctgtga ttcctccctc cccactttct ctggctaccc acaccctgcc
16501 agggccttga gacttagaac atagaaatta aaagaattta attccaatga actcaaaatc
16561 cctgaagctg aaaccagagc attctttgtt gcttgagaaa gggtagagga gtttagggaa
16621 gagagaacta aacctacgaa agacagtcac ctttttccac atctcgtccc tcttgctgtt
16681 gaagtcgcct gtgcctggga tgtccaccag cacgacccct tctgggatca ggtcggattt
16741 gggaagtgtc acttccacat gtttgatcaa gggccagatg cgcatctcag cggcctctcc
16801 atcccaatct ctcctctgtg tgcggatgta ggggtccagc ttgatggaca gctcttctgc
16861 ctgaagaagg aggacagagt cacacacacc agccatgcac ccagctctgt tcaccccggt
16921 tggctgtgat gcaggttcat ggtaagtatg ctgagtaagg gtaagaagtg cgtccaacag
16981 gaggcctgca atcaggtctg taggacctag aacctgagag ccaggaagga ccctggagag
17041 gagcaagttc aagatcctta ccttacagat gaaacaaaac caatgtcagc taaaatggga
17101 ctttagggaa gttatagtat tgctgaataa taagtttatc ttctaaactg cattcagttc
17161 taaaattaac atactatgta attgaYattt tcattaccag aaagctagca atgactatag
17221 aaaattaaca gtgatatggt aaccatattt tccaaactga aaattgatct gaaattggat
17281 cttttttttt tttttttttt ttttttgag acagagtctt gctctgttgc ccagRctgga
17341 gtgcagtggt gcgatctcgg ctcactacaa gctccgcctc ccgggttcac gccattctcc
17401 tgcctgactc cccaggagct gggactacag gcacccgcaa ccacgcccgg ctaatttttg
17461 ttgtattttt agtagagaca gggtttcacc atgttagcca ggatggggtc gatctcctga
17521 cgttgtgatc cgccctcctc agcctcccaa agtgctggga ttacaggcgt gagccaccgc
17581 gcctggccga aattggatct taaaaagagt ttttaaaatt tatcttctga ttacaaaaaa
17641 taccttgata tgtaggcatt tctagaatat tttaatgatg gtgggtgaga gagggaatag
17701 ttcttagacc acggttccta cttaaacatg tctcgggaca atgacacatc catgccagca
17761 actatgacag taaatcgcaa ctggggtact tcagaggaca ggggatttgg gatgtatggt
17821 ggtcactgtt aaataaattt ctataaaata gtcctgaaag aaagataaga atgtcagttc
17881 ttaagagagt ttaaattaaa tcgctggatt tgttgcaatc tggggaagga gtaagagatt
17941 tcatcaattt caaccaaatg ataaaccacg acggaggaga taataaaagc tctttaagac
18001 attgtaattt taaaatagag cagataccgt aagagagaag cccaggaaaa ggcaggggct
18061 tgaaaagccc cttcctacaa gagggctcag cccaataaac tggttccggg caaacatcgt
18121 tgtagaaggc cttgattcta ggatctccag tggaaaccct gaatttgtaa gcccactcat
18181 cgagatggta attctgttca ccttgtttcc gtgcgtaaat ttatgacgct gggaaggagt
18241 atttctaaat atagagttgg caaagacgtt gataccсttg tgtaagttgc gtgtattcag
18301 ataaagcaac tagttttgta atcattgtgt ttcttagaca tgctcagtct atgttttaga
18361 tattagaagt gtaatcattt taatagtaat attcgtctta aaactgtaag aaatgggcac
18421 tgtatttgtt tgattttcca ggtatgcaag agatagtaac atgctttgaa aaggtttcat
18481 tcatttgatt tttaagtgtg cctagtcaag catttaaaca ttttaagagg ctcaagtata
18541 ttgaacttta actgtaatgc aaaaagccta aggaaatgtg attaattatg taagtatcat
18601 taatatttaa ggaagatttg ctttgttaat caggagatca ttgaacattt aactttagga
18661 catgtataaa aattgtaccc attttaccaa taatcactag atttataaat agaatagcaa
18721 tattttaaag gtgtatttaa aggtgagaga tacaagaaaa actaggtttt taaatgtata
18781 gctttcctaa attgaatgtt gattccacaa atattttgtt ttaattcaga aattgaattt
18841 taacttaaaa taaacattgt ttataaaagc aagaatatca ttctactagt tgcctatcga
18901 atgtccatcc tgtccctctt ttatgccagc agaatcctga ttttctgtct gactggggag

```
18961  gcagtggagt gaaactggtc taagcaaatc atgacaagtc tgcttttcac tttctctgga
19021  ctcccttttca gccaggaagg gctgtgtggc tcagttctga actctgaaat ctacacagaa
19081  atttgtcaga ggtatttctg ggaaagtttt tactttctga tgaaagggga gatgtggctg
19141  atgccaacct tttctccact tcttccttcc aggaggctag catgaagtct agcactccgg
19201  gagccatctc atgacaatgg gggcgacgga aggcaaaggg agccagagat gctgatgttg
19261  gcattgctga tccactaaac caaccccacc cctactgccc ccaaacctct tacatgagaa
19321  aaggaataaa tccctgtttg tttaagccac tataagtctt cttaaaaaat ctttggcagc
19381  ccaaactatc cctaattatt ctcaagcaac tgtaaatagt ctttttctgg gcataagagc
19441  tcctccattc acataccaaa aatttccatt tgatagccat aaataatgag gataacttgg
19501  gctacggata cttctaattt gggtagcaac ttatttctta tttcacacaa acactgtacc
19561  acaagcccat cccctgaaac aggttcaact gttagacttg agacccagga tgaaatcaag
19621  gaaaaaacga acttgacgct acctcttccg ccttgagggt gatgactctg gaggtgggga
19681  tcttcctttt gggcttcgcc ctcagtaact cctcatagtt cttactctct gccccatttc
19741  cataaatcat ttgtagcttc caggtggctt cctccactgc ctcatcccta ttccacgcat
19801  ctgcctcttc tctgctcagc tcctccgtcc tatgcaggag tttggtcagg ttcttcagct
19861  cctccctcca ctcctgccaa ggcagagtag ggccaagccc ctcttgacac agacacagag
19921  aacaccgaca aacagagggg cccattgccc cctgtggagg gccagggggc tgcatattca
19981  gaaaatctag gtcatctatc tggggtctcg aagaggggaa tggcttgccc aaagtctcat
20041  aaaaatgcaa ggaccaggct agaccccctc cccagctcac ttgatgaact ttctcctggg
20101  atgggctctt ttcattcaac aaaggcatga gctgtatttg caaggaatat aatgttatct
20161  ctgagagaca gtgagaagga aagaaagaaa aggaagaaaa aaaggaagag aaggaagaag
20221  gaaagaaggg agagagggag ggaagaggaa ggaaggaaga aagaaaggaa ggagggaacg
20281  aaaaaggaag aaaggaagga aaaaggaagg aggaggagga aggaggaacac
20341  ttacctggtc agacagaagg tggattttgg cctcatactg cacacagcag ccagagctca
20401  cttgtacaat gcaggaagta catatgcttt ctccagacac tggtagaaac attgcttgct
20461  ggatgatggc attgatcagg gagctcttcc cagccctagt gcttccaaat aatgcaatgt
20521  agattgggtc cactgtcggc ttttcaatca aggcaagaag cctatttctg gatgaatttt
20581  aaaatgcaca ttgccatgat catcaaagtt tagagtgaag agcattgaaa cagaatgcaa
20641  aggaactgaa ttctaatccc gggcacgtca ctacaacctg agtctctgtt ctctcctctg
20701  tcaaaggaga atatcaatcc ctgttgacca cacagagttg gcctggggat caaatgagat
20761  tatgtaaaaa tatttggtaa tgataattcc acacaatccc tgtaatgtct atatagatgt
20821  gaggtgtctt tatttgtatt cactggaaat tgcatattct ttttttgtt tgttttatgtg
20881  tctgagacag gatctcactt tgtcacccag gctggagtgc agtggtgcaa ttatggctca
20941  ctgcagcctt aacctcctag gctcaagcga ctccttcgcc tcagcctctg aagtagctgg
21001  aactacaggc gtgctccatg acgcctggct aatttttttg tatttgtat agagacagag
21061  ttttgccata ttgctcaggc tgctctcaag tggtccaccc gcctcggcct cccaaagtgc
21121  tgagattata ggtgtcagcc actacacctg gacagaaatt gtatattctt gatcctagaa
21181  atacaatgta tacagacatg aagtattaat agtgttagga gcaacacaga gtcttactga
21241  gcaggagaaa ttgtagcctc agcaccactc gagtccttca agtcagcaga ggacaaataa
21301  ttggggacat gagctcagag tcacacagcc tggggtgaat tctggaccct ctcactgact
21361  actggtgtga gtttgttcac atctgggcct ctctgagcct caatttcagt aaaatggaag
21421  tgatcataat agctcctact ttataggagt gttggatggg ttaaatgata tttgacatat
21481  ataaagcact tagcagatta cctaacagtg acagctcaat gaatggcaac tatcccatag
21541  ctacagaaat ttgtgtccct cttttcttag tttctaatta aatagtccct ttccttgttg
21601  ggggaaagca cctataatcg cctaaggaaa gacactgaca taaaatttca gggttgcaga
21661  tttcagactc acatgagata cttgactcca ttagggatgc tgtcatccag gaagacagac
21721  tgaataagtt tctgataagt gttgctcaaa accctctgg tccgtgattc caattttcta
21781  tctggaatta acagagagat gtcacctgca ggtacctggc agggataaag tactaggtct
21841  ccaaaggagg tgtctgttga acatcgcaga gaagggaaaa aaaaaatgaa atgaaaagcc
21901  gattaaacaa gatagcaggt tatctcacac gagggatggc ggctcactgg agatagcaat
21961  cattggttct gaaaatctcc aaagagccag gctgctctga aactctggta acagaagtta
22021  tggtatgctt ggccacgggc ttcagcccct tctagatttt tccctcctgt ggtcataaaa
22081  agaaagaaaa aatgcaagga caccatgctg acaccccacgg aagcaccaac ctcatcattt
22141  tcacaggctt tgttctaatc tggaagaagt tattttgata acaaccctcc tgcccacaga
22201  tgcctggaga caaattgcct aactgcatac cgctacagag actttgagcc ctctctttcc
22261  aaaacaggtt tatttgatgt ttcatccagc ttcagaattt aacctcctct tcctttgacc
22321  attttaacat acttggaaca gaaccgaacc atgttaaaac aacagttcca agacactcac
22381  atttcttaag agcactctgc tccatggagg gaaatgctcg gaacccgctgg tctcgatctg
22441  atttcctttct ttttctcgtt cgttctttat ataatcatcc ttcaactaga gataaacaga
22501  ggatatataa gattataggt gttggggtat ggtatttctg cctcacctct atcagcatag
22561  aaactcaaag ggtctaacag actggctgtg tgcagtggct catctgaagca
22621  tgagggatta catgcctggg agccaaggt gggaggattg cttgaggtca ggagttcgag
22681  acatgcctgg gcaacacagc aagaccctg tctcaaaaaa aaatttttttt ttttggtaga
22741  gacagggtc ttactgtgtt gcccagcagg ccagagtgct gcggcatgat cacgactccac
```

22801 tgcaacctca acctcccagg ctcatgtgat cctccccacct cagcctctag agtacctggg
22861 actacaggca cacaccatca cacctggcaa atttttgtag agacagtgtt tctgtatgtt
22921 gcccaggctg gtctcgaact taccaaaaat atatatatat atatttttta attagccagg
22981 tgtggtggtg tgcacctgta gtcctagcta ctcaggaggc tgaagtgcga gggtcacttg
23041 agcccaggag ttgtaggctg cagtgggcta tgattttgcc actgcactcc aacctgggtc
23101 atacaagacc ctgtctcaaa aaataaaaaa ataaaaaaat aggaactgct tccagctctg
23161 tctgcccata aactcatttg ggaaaaaaca ctgttggatc attccagttt ggttcctact
23221 tctcagagtc acaagactgt ctgcatttag ttccaaaatg tagagttcaa tctatctccc
23281 cagataaata gtttctattt gcaactcctc agaagccaaa gtggctggac attcttcacc
23341 aaatgccaag tcttaggaaa tcaaccaact gtgtagagaa aagctgaaga cggggttaag
23401 tgtgcagtga ggaaaggcct ctgggaggtc tttccagact aggaaagaaa gcgactagaa
23461 gcagaatgca aaggaaaaca ggggccaggt gaccagaaaa aatcacatct tcttgagcct
23521 caatttattc atctggaaaa tgagagaact gacaaaaaaa atacacatgc attacaagag
23581 tttggatgga tgcccttcag agatccttca aaatttgggg aaatttttta cctctcttac
23641 ttggagacat cagcagttgc ttccttgcat aataagcaag aacagaaatc acctagaagc
23701 agatctttgt agctctgcgg agattcattc acttaagcag tttcccttgg ttatgaagtg
23761 aagggcttgt tgggcccatc atcctaaaga aggggtataa ccaaaatgtt gtgttttaga
23821 tggattttag aaaacacccc ctggtcatgt ttacctggct agaaaggggc aagaggtgga
23881 tctttggggt gaaggttgtt gaaaatggtt ctaacccagg gctcctgggg ctggcctgca
23941 ccttagaaaa tggccatgag gtgaaccaaa agagtagatc cccaagaatc acagggaggc
24001 catgaggctc caaaactgag tgtgacattc tgaggtcatt ccctgcagaa tcacagagaa
24061 gaaatgtcac gtggcatcca agaacggcag cccacacaga aggcccagtc tctgcctgag
24121 ggctccagac acagatctcc cagacaattc aggcagccct ccctctctgt tcaaccttgc
24181 atcttccagt agaaatggaa gccaacgcac accccgtaga atattctagt gcaagccatg
24241 ctcatttgcca aggcctgaat ctctgccacc tcatgctcca cgctcaagcc acaactgaga
24301 gttgagagag gttatactc gaccctttcc tctcagacat tctaactgat gattgagctc
24361 aaattcaaga attcgccctg gctcggtttg aggactgcct tagaactaaa taccaagtgg
24421 ttgctggctt ggtggctgga gctggagagg aagaggcaaa gaaagaagtc tgctggtcag
24481 gcccctaggc cagctaccgg ctgaagaaca ctttaatctg tgctcgaaaa agcatctcag
24541 aactccagga tgtgtccaca acctgtctgt ggaaagagtg gaaaggggatg tagacttttgt
24601 aactcaggaa ctcttttggg taaacaatgt ttgcctaatc tcttagccat gtgtataaaa
24661 caagggccaa gtccacacat ccagggccct tatttcaaca ttgtaaggac tggcaacgaa
24721 tctgataaga gtttggaagc ttatttctca actaaagcaa atgctaggaa gtccaataca
24781 gcagggttta aaacttttttc ttcaatttct aaaatgcaaa actatctgga aaggagaaag
24841 tattccatct tggatttata ccatacgagg gtagtatttt tatattagat tgtaaccaaa
24901 ataaacttgt ccgatttag atcacagatc ttattatttct tgtccatcgc tcaagccctt
24961 ccttgccctt tccagcattc tccaccgaga aaccagctgt tgggtggtgt agcggcagtc
25021 caaaaagcSt agtatactgc tgctgttcct tcttgctgcc acaaggtgtc agttttgaaa
25081 actgatccc caacagcctg agctgagatg Yggtttcatt gttgactgtt gaaatttttt
25141 ttttttttt gagacgaggt ctccactctc gcccaggctg gagtgcaatg gctgggtcac
25201 ggctcactgc agcctcaacc tccgtggctc aagcaatcct cccacctcag ctcccaagta
25261 gctggaacta caggcactca ccaccacgcc tggctaattt ttttttcttt ttttttttt
25321 ttccagtgat gaggtcttgc tgtgttgctt aggctggtct tgaactcctg ggctcaagag
25381 atcctcctgc cttggcctcc caaagtcctg ggattacaga catgattcag accattgcca
25441 gaaactgcca gaaatcttcc aagcaaaacg atcccattcc tctaggctaa gctcaactga
25501 ggtgacccca aagtggcagc tcttcctata tgcctgctca ggcttgcttc agatgctagc
25561 atcaccccca ctaacccaga aacactgctg cactttgccc ctaaggaaat ccatcccctc
25621 ggagtgagga aacattccct ctccagttct caaaacacaa aggatatgat acagccactt
25681 tttctgcaac tgggggttat atccctgtca tcgtcctata gggaagcctc ccttattggc
25741 tccagggggcg caataccagc cttctgaggg agggaagcca cccgcactga ctccaatgtg
25801 agtcaccctt ccaggagccg ctccaaggca cctacatctc tcctttctacg gaaagccgcc
25861 taacgtcatt ccaggggtct tgtaagacag gctacctgac tgtgagacag agtccaagct
25921 gactttctgg aacattatta ttattgagat ggagtctcac tctgtcgccc aggctggaga
25981 gcagtggcac aatcttggct cactgtgacc tccgcctcct gggttcaagt gattctcctg
26041 cctcagcctc ccaagtatct gggactacag gcacacacca ccacacccgg ctaatttttg
26101 tatttttagt agagatggga tttcaccatg ttggtcaggc tggtcacgaa cctctgacgt
26161 catgtgatcc acccgcctca gcctcccaaa ttgctgggat tacaggtgtg agccaccatg
26221 cccagcctgg aacttttttt ttttttttta aggaaaaagc cgcacttatt taactgctgg
26281 ccaaacagtt cacttcatta tgaacaggtt attcagttca ctgttgaaat atctgatctt
26341 cattcactat ttaaacttgt cacgagaaag caccttctca ataaagagta aggaacaatg
26401 acaacagtga aatatagtcc caacctattt gccttttatc ctatatcagt aatcagttcc
26461 tatatcctcc atcagaagat actgcaaaga tgttacctgg atgcggttcc tggccaaaaa
26521 catccttcgt ttctgccatt ccttgttacg tgaactcctg ctcttctcag ttcaggagaa
26581 ccagcctgtg aagacaaagt acaaagacag gtggggcagc ggaatttgaa aatacagaaa

```
26641  gcaaacccta aggatgtgtc agtctgcttg tgcggtattt ctgcccattc caacgtatct
26701  ctgaatccct cacaacacct agtacactac ttgatggaaa tataacaaag attagtgttt
26761  gaacactggt ttccaatata acttaggcca ggcgcagtgg ctcatgcctg taatcccagc
26821  tctttgggag gccaaggcgg gaggatcact tgaggtcagg agttcaagac cagcctgacc
26881  aacatggtga aatgccgtct ctaccaaaaa tacaaaaatt agccaggcgt ggtggtgggt
26941  gcccataatc ccagctactg gggaggctga ggcaggagaa tctcttgaac ctgggaggcg
27001  gggcttgtag tgagccgaga tggaaccact gcactccagc ctggatgaca aagcgagact
27061  ctgtcttgag aaaaaaaaag agtctaaacc agtattacct gaggagcttta gggtaactca
27121  cgctgaaatg agaataagcc tctggtgacc agagctgtga aggtgaattt atatagctcc
27181  gctgctttgg gtggcatcag tgctccactg gggcaaggct tgaaccctga gccagtgcta
27241  tttagttcca gaaagtctca gcaggaatct gggaggtgga acattagata ttcctagagt
27301  tccctggagt tgctttgggg ggctgctgac tggggaagga gatgcagtga cttggttccc
27361  tggacctttcc tcaccaagcg caacttccac caggaggaca cccctcctgg gctctccttg
27421  cagcttgcag catggagcat ctgcaggagg gagaggagag gccacatccaa aagaagaagg
27481  ggcagatcca gttggtcttcc agtccaccag cagatagggc ttggacatag agggagaact
27541  ggacccgtgg aggctcagaa cagagggcac tgcccagaca gggtagaatc tgctagcctg
27601  gagctgcttc atctccaccc atagagaaga atttgaggaa cacgagtggg gaacacccaa
27661  ggtgcttact tgccgttacc tgatgtttct gttggatca ctcagccgtg tatttcaaaa
27721  gcagagtcac cagcccttct gaaatatgca aaatcacctt tgatctgtcc tactagaccc
27781  acaggctgtt atttagggaa actatgtctc atttacacat taaccccaaa ttaaaatcac
27841  cattcatcag ttactcttag tttggtttgc agatattaac tgactaaacg gcttctgtat
27901  ttggtgggtg ttgggtgaat gggggtgagaa cccctattaa gtgcaagatt ctgagtctta
27961  ggtagagctc tttccctctc ccttcctccc ctctgcagcc cattttcaga tcatccacca
28021  ctccttacag ttctccaaag cagggtatcc tattgaactg ctgagcattt tagcacatgt
28081  ggggtgccct tccctctctc tcgcaggtga ctgcttgctc ttgcttcaaa atcctgttct
28141  agtgttctcct ctgtgaaacg gtgtctgatt ccactcatt ccccccgtgt gtcccgcgct
28201  ccatacacac ctgtgttata acactgactg tgctgtgctt acgtctgttc ctcctggttg
28261  aaccactcga ggtcagagga ctgcatttttt ttcagtggtg catttctatc aagaagggca
28321  atgactaact aaacgttagc tgaatgaatg gataacataa tggatgggaa gcttttgatg
28381  agattccaca ccaaaggatg tttaaaagct aaatttgttg ttttggtctg gtggtttgtt
28441  tgcttgtgac agagtcttgc tctgttgccc aggctggaat gcagcggcac aatctcagtt
28501  tactacaacc tccacctcct gggttcaagc gattttcctg cctcagcctc cagagtagct
28561  gggattacag gcattgcacc atcatgcctg gctaattaca attttagtag agatggggtt
28621  tcaccatgtt ggccaggctg gtcttgaact cctggactca agtgatccac ccacttcagc
28681  ctcccaaagg gctggggtta caggtgtgag ccaccatgcc tggccctgaa ttcatttttg
28741  gtatgtaaga gtccttgatt gaagagtaaa gcaaagagta gaaataaata gtcaagtatg
28801  caaatgaagc Rgcactcaca gtgaggactg ctccacgggg atgaggaata tttgatgtga
28861  ggWagggaag acacaggtaa aggcatgaaga tgggggcagg ggccttcatg gtggtcttca
28921  aatgcattac cttacagctg caaataaaag agacatcctg catatttttct agggttccca
28981  gagggtagaa atagatccac taggtggcag gtacaagaaa gcattttggt ttaacattct
29041  caactaatca gagttgtcca aaatggaatg agctccctta ggaaaccgtg agttttctgc
29101  ctctagaggt gtctgaacct atattgatat gaccacctaa taacgacatt gagatagata
29161  aattttaagc cttcttcaaa tcccaagatt ctatgttctt acttgaaatt tcaccaaga
29221  aagctggtag tagaagtgcc ctatgaggtc accaaatttc acaagaggca caagcaattt
29281  ctggtttgga atactgagtc agaaatgctg acacacatca aaacctaggt gagctacaag
29341  aaaaaaaaag gtagatgggc tataacatga gtaaatatac cataatgcat gtcaataatt
29401  ttaggcaggg tgtgatggct catatctata atccccagcac tttgggaggc tgaggaggga
29461  tgattcattg agccctggag ttcgagacca gcctgggcaa tcaagtgaga ccttgacact
29521  accaaaaaaa aaaaaaaaga aagaaagtag ccggttgtgg tgacacacac ctgtagtacc
29581  cactatttgg gaggctaaga tgggaggatc ccttgaaccc tggagttcaa ggttgcagtg
29641  agctatgatt gcaccactgc actccagcct gggtgacagc aagaccctgt ctcaaagaaa
29701  aaaaaaaatt agatacagaa ctaggattac ccctaggaaa aagatctgtt gttttctgaa
29761  gagagcagct taaggagtaa ctcgtatgaa atgctaggca tcatattatc acagtgagca
29821  ctggaagcaa aacaaaatgt atgatacaac cagtgaacaa atccatggtc gacctccagg
29881  acagctggtg tgctggaatt caaattctag gaggaaacag tggagccgga taaagtacaa
29941  aagaactgat agaccaagtt gataagagtc gtggtcatac agacactaag attagggacc
30001  ttcaattgag agagctgtgg attaaagggc acaaaatcaa agggccttga gtttagagca
30061  gaagcagctg tggtcactga attctggaat acgggtagta gttttggctt ctttcagaat
30121  cacaagaact ttagttcatt tgactctcatt tactaaatca acagtacaca gtgtccagca
30181  agggccgtta gcatgtaact agctgggtt ggtttgggtt tagctgcatg caatgaagac
30241  agaaaaccac acaacttcct ccgtagcagc atctagggtt tctgtataca agtaatttgt
30301  gaactctaac tgaaatttgg aatcattgga aattatgtgg tttggttgtg gtggattggg
30361  cttcaaattc ctttggccaa tgttccaaga ctggcaggaa gggatcattt gatgaccaaa
30421  caaaaacact agcaaatgga aagggatcat ttgcaaaaag gctaagagga cagaagaaaa
```

```
30481   taaacaccaa gtacataaaa aggaaaagcg ataaacaaat gggggtagtt tggtacagac
30541   attcagtata tagtcattgg gttgaactaa atgatgaggt gggaagaaca ttaggctgga
30601   aatctggtgt ggaagcttcc agctccagct ttaccaccca tcaataaagc tggaggactt
30661   aagacaagtc gttttatcac cctggcctca ggtttcccat gtgtaaggca aagactgaac
30721   tagtccttaa agtgtgagtg ttctctgatt tagatgggtg ctaaaaagac acaaattctc
30781   attttgaaaa tgtcacctgt cattgaaaMt gagaccgtac caatgattag ggcttccgtg
30841   tggccaagag cagtacacca agagcactgt gatttcaagt gcattgtatt aaggagaaaa
30901   tgagctacag gagtatagtc ctcttcaaa tcatcctgca gtctatttcc ccccaaagag
30961   aaggaatggt ggtgttcatt gtgaaaattt ggtttctgtg gagaagcaat tgataacagt
31021   ccaaatttat tgctcagata agcaaggttc tgcctgtgtg gtttattttg cttgtatttc
31081   agctatgtgg ttagcactga agttttgctt ttagtgctta tttacattca tgtgcactga
31141   acctaagaat agcatctttt aaataagact gtgcacattc agctagatat aggaaggctg
31201   cacagaactg atttcctgat aaataattgt aacttttcac agttattctt gcttctctcc
31261   ccctcctttt cttctgttg tgtttgctta ttgttttttt tcttacagga aaatcacaga
31321   ggcaacacaa acgcaggtca ttcctgtact agaacagctg catatcatgg cattgaatga
31381   agaatgcggg ccgggtgcgg tggctctcgc ctgtaatccc agcactttgg gaggctgaag
31441   caggtggatc acaaggtcag gagtttgaga ccagcctgac cagcatggtg aaaccccatc
31501   tctactaaaa atacaaaaat tagcccggtg tggtggcacg cgcctgtaat cccagctact
31561   caggaggctg atgcaggaga attgcttgaa cccaggaagt ggaggttgca gtgagccgag
31621   atcacgccac tgccagcctg ggcaacaaag cgagatttcg tcttaaaaaa aagaatgcta
31681   gggccccttc ttctacagat ccagaccctg aggaccagga aggggaagaa acttgtccaa
31741   ggtcacatag taagattatg gcaatgaggg ctgaaactca gttttcctga ctccaagttc
31801   aatgttcttt tcatcacatt cagcagcctc taataggcac ttattaaaca agccccctgg
31861   agctcaggca tagggcaatg gaaggagtag tgcccgcaaa ggaggttcc ctcaaatgca
31921   tggcaaaggc atttcatgag aaggaaggct gttgagtggg gagagagagt agcaacttga
31981   tagaattgta tgcaggaact gaagctgaag gtactgcctg caaactgcct tttgttttt
32041   gttttgttg ttctttgttt ttttgtttgt ttgtttgttt gttttgagat ggagttttg
32101   ctctatcgcc caggctggag tgcagtggca catgatctca gctcactgca acctccgcct
32161   cccaggttca agcgattctc ctgcctcagc ctcccgagta gctgggatta caggcacctg
32221   ccaccatgcc cggctaattt ttgtatctct agtagagaca aggtttcact atgttggcca
32281   ggctggtctc gaaccccctg cctcaggtga tctgcctacc ttggcctccc aaagtgctgg
32341   gattacaggc atgagccacc atgcccaacc ttactgcctg caaacttgaa gacaccctca
32401   gaagtaaaac aagccagaga gagagagaga gactatcaga ggaatacatt ttcactgcat
32461   tttttctgtg ttcaatgcaa aattcaatgt gttttattaca aatgacaaat gtcttttct
32521   tttcccctag ttatctctcct taggcagaat ctcatttcac cctaccttgc ctcgcatcat
32581   taacccttgc caacactatt tacttactta aatttaaatg cttaaattag caaagtcttt
32641   caaaggggca ttttggtcat taacattggt ttactctcta ctttaataa atatgggaag
32701   tacttggtac acagcaagca ctaaataatt tgttgaatga atgatgatag atataatttt
32761   ttgtatctat atctagatag atctatctag atctagatat agatatatat cttagatggt
32821   aagatcaaga atagcagaaa ttatatttac tattttattt atccatccat tcattcaaca
32881   aatatttgtg agtgcctatg atgcaccagg cactgttcta gatactgggg gtacagcagg
32941   aaacaatgtg gtcacagtat ctgcaaacaa agggcttcca tattccagat gtgaatggtg
33001   gagcaaaaat tattagggat ttggagtcag aatgcctgga tttttgctcc tgctcccaat
33061   cttcaatgca acacagagca aatcacctga tctctctgag cctctatttc tccacatata
33121   ggatagaatt ggttttaaaa aaaatacctg tatcaagaat tcattggcca ggcatggtgg
33181   ctcatgcctg taattctagc accttgggag gccaaggtgg gccgatcact tgaggtcagg
33241   agttcgagac cagcctggtc aacatggtga aaccctgtct ctactaaaaa tacaaaaatt
33301   acctgggcat ggtgcaggcat gcctgtaatt ccagctgctt ggagagactga ggcaggagag
33361   tcacttgaag ccaggaaaca gaggttgcag tgagttgaga tcgcaccact gcactccagc
33421   ctgggcaaca gagcgagact ccacgtcaaa aaaataaaaa ataaaaaaga gttcgttgtg
33481   agaattaaat gtgataatga atgcaaaatt gctctgcagg cacttatgca tctgtacaaa
33541   tgttattttt tgaatatttt atgaaggtag ttaaactaga aatcagtact agtgtcatcc
33601   aggccacgtc tgttagtctt tggggaacag atgcccacctt agctgagatt ctgactccg
33661   ttcttgtccc tattgatcaa acacattgag gatgctctac catcttcctt aaagaatctt
33721   cgatcagctg ggtgcagtgg atcacacctg taatccccaac attttgggag gctgagccgg
33781   gcagatcatg aggtcaggag tttgagacca tcctggctaa ctcggtgaaa ctctgtctct
33841   actaaaaata caaaaaatta gccagccgtt gtggcacatg cctgtagtcc cagctactca
33901   ggaggctaag gcagaggaat cgcttgaacc cgggaggcgg aggttgcagt gagctgagat
33961   catgccactg cactccagcc tgggcaacag agtgagactc catctcaaaa aaaaaaaaaa
34021   caatctttgg tcaagttttt tcttgctctc acaagaaggt gagctgaaga atgaaagaag
34081   gaagaggagg agactgttaa tgaaatgata gaatgttgat gaaatttaga atttatttcc
34141   tttctctttg agtttgggtt taggtttaag taactttggt gttggcaaca tttcctaacc
34201   acctcgttgg ccactgcact gctcttccaa actagggatg tcccaaggca gcaatttaaa
34261   cacattagct cagaagcaaa agtgaaacaa gggcctccaa atctctaaag gaaaagaggt
```

```
34321  atgttttcag cattaacaca tcggctaatg tgttcagaat tagaaatgtg gccaccagaa
34381  gcagtcgtag tagaaggaag gctttaggat gacatgtttt tctccatctt tcttccctag
34441  gtaaagaggt aagcaaaata agcagatatt ttcataacgt actttagcag attctagcga
34501  aacgaatttg aatcttctca tattgctctc ccaagcttgt taaagctaat gaggcataag
34561  atgacacttc cctcctatc aggaattcat acacctgcca gcaatttctg caatagctgt
34621  tttcttttgg gaggaatgat taatgacttg cctaagatca cactgttctg taaaatttcaa
34681  actaaaacct gattctcccc atttctagcc cactggcctt tttacatagc cttaaaattc
34741  acttaaacag cctgagcatg gtggctcatg cctgtaatcc cagcactttg ggaggctgag
34801  aggagagggg atcccttggg cccaggagct tgagaccagc cttggcaaca aagtgagacc
34861  ctcatctcta caatttttt tttaattagc tgggcatggc agcatgtatc tgtagtccca
34921  gttattcagg aggctgaggc aggaggatta cttgagccca gaaggtgaag attacagtga
34981  gccatgttca taccactgca ctccagcctg ggtaacagac cgaagcctca aaaacaaaca
35041  aaccaaaccc ccaaaattca cttaagcaaa cagaaaagta aaattcactt tccctcaaga
35101  aataacttgc tttaagaaaa tcaaaggaga gagaaggtac aaatgtccca tatacagaag
35161  aattccaaat aatttacgta gctactccat cctcaaggag gtagaataaa actcccctgct
35221  ccttaagtgt gtgctgtgca tagcagcttc tttccaaaga gaacacggcg gagattggag
35281  cagggaaagg atcaccttat agcagagaaa ccagacaagc gctgcctcta ccaggtggtc
35341  aaggtcaaca ccaacagtcc taaatcatgt tgacaatatt atcccttgat atgatgtgat
35401  gagaacagca ctttaactct gggactcctt ccccaaaacc cataactcca gtctaataat
35461  gagaaaaaca tcagacaaat gccaatagga gaagcctaca aaatacccaa ccagtactcc
35521  tcaaaactgc catattcatc aaaaacaagg aaagtctgag aaacaacgct acagctaaga
35581  ggagcctaag ggaacataac taaatataat gtgctatcct gataggatgc cacagtagaa
35641  agcagacgtt agataaaaac caagaatctg aatccaagcac agacttttagt ttaagaatag
35701  cgtatcagta tcggttcatc agttgtaaca aatgtaccac actaatacaa gataatgggg
35761  aagttgggtg ggaattacat gggaatgctc taaactatct tctcaatatt cctgtaaact
35821  caaaactgtt ctaaaaatta aggtccattt ttaaaaatc aaccacaagt tacagtacaa
35881  attacataaa agaaacaact taccagatgt cactgaacag aaaaaaaaaa aaaaagttct
35941  ggtttggtta caggagtcca cagaggagat ggtggcagct tctccttggt tcaggtattt
36001  ggaaccagct ggggtacgta gccctttggg ccacaatcac aaagccacgt ttacacagca
36061  gaagtgaaac caacttgcca tcagggagct atttaccatg gtctcctccc acagatactg
36121  atttattctg tcttctttca cttaaatcta aattcaccag gcacggtggc tcactcctgt
36181  aatcccagca ctttgggagg ctgaggcagg cagatcactt gaggtcagga gtacaacagc
36241  agcctggcca acatggtgaa accttgactc tactaaaaat acaaaaaaaa aaaaaaaatc
36301  agccaggcgt ggtggcagaa ccctgtagtc ccagctactc aggaggctga agcaagagaa
36361  tcacttgagc ctgggaggtg gaggttgcag tgagccaaga tcgcgccact gcactccaac
36421  ctggatgatg gagcaagact acattctgaa aaaaaaaaaa atctaaatgg tacatgaaac
36481  gggcatcttc caccctctc tgccatgttc ctacaagtag acagatgtct ttttcctttt
36541  ccaagtgcat cactgcatcc ttccacagca tcttttctct gagggtgaac aatattcaga
36601  tgactggttc actggagcag acaggaaaaa tgccccagtt ccaagacaga caaagcactg
36661  gctccccgac acccaactat aagacatgac tgggagagat ggaggatatg agataataaa
36721  tataaagtta ttcttgaccc aaagtcttaa aattcaccaa aaataacatt tgccaaaaat
36781  aaaacaacat tggattgttt gagtgtagaa atgagtgata taccgcttta cacctctttc
36841  tggaacttaa attttaaatc cgtatatttt tatgtcttta tttagttaga gacaaggtct
36901  tgctctgtca cccagcctgg agtgcagtgg cgtgatcata gctcacagca gcctcgacct
36961  cccaggctca agccatcctc ccacctcagc ctcctgggta gctgggacca tgtgtcatgct
37021  ccatcacgcc catctaattt taaattcata tttttaataa acccagaaaa caaaaatttg
37081  aaagtgctgt ccaggagaga agaaaataaa acccactcca ctttgctgtg tctggcaacc
37141  caaacgatca catcacatac aggaaaaaaa ttgtccttg aaccctcagc ttcaggtgt
37201  gtgttacctt ttttttttt ttgtgagaca cagtcttgct ctgtcaccca ggctaggtg
37261  cagtggcgcc gtctcagctc actgcaacct ccgtcttccg gttcaagag attttcctgc
37321  ctcagcctcc tgagtagctg ggactacagg ggtgcgtcac catgcctgac ttttttttt
37381  tttaatttta gtagagacag ggtttcacca tgtttgccag gctggtctcg aactcctgat
37441  ctcatatgat ccgcccacct tggcctccca aagtgctggg attacaggta tgagctactg
37501  tgctgggcca agggtgtatg ttacctttaa aggccaactc agtcattacc aagacaacc
37561  tcagtactct aggtatgtat ttagtctgaa gaggggattc agaaggtaaa gaggtcagaa
37621  cagggaaaga attgaagata aatgtttaga ctgtggttct aaaaactgct ttgaacttt
37681  ggcaagatga cgtccctcct ccatagaaaa accacagaaa caccaggcta aagttcagaa
37741  caaagaaagt cagcacaaat gccatcctgg atgctgagtc ttatactgat ctctctaggc
37801  aaaatcacac cttacgctta catttcatgtc acgtgtggctc agctctccct ctactgggta
37861  tttcttagct tcaacagtta accacaaatg ctactaaatt acttaattat taaaattaat
37921  tttgagcatt tttaaagctt cctgggcaa ggcccagtgg ctcacacctg tgatccctgc
37981  attttgggag gccgaggtgg acagatcacc tgaagtcagg agcttgagac cagcctagcc
38041  aacatggtga aaccctgtct ctactaaaaa tacaaaatct agccggtcat ggcagtgtgt
38101  gcctgtagtc ccagctactc aggaggctga ggcaggagaa ttgcttgaac atgggaggca
```

38161 gaggttgcag tgagccaaga tcaggccact gcactccagc ctgggcgaca aagggagact
38221 ccatctcaaa aaataaaaaa ataaagcttc ctgagttcct ttatttgttt gcttgttttt
38281 gtttgtttgt tttagacagg gtctcactct gtcaccccag ctgaagtgta gtggcgttat
38341 cacggctcac tgcaacctca acctcctggg ctcaagtgat cctcccacct cagcctccca
38401 agcagctggg actacaggca tgtgccacca cacttagctt aaaaaaacaa aaaacaaaaa
38461 aagaaaaaca aaaacaaaac aaaactttag tagagatgag gtctccttat gttaccagg
38521 gtgaactcaa actcctgagc tcaagcgatc ctcccatctt ggcctcccaa agtgttggga
38581 ttacaggttg aagccactgg gtccagcctc tggggttctt tatggtagtc cttggcacct
38641 gctattggac gcctgaatgc taggcctgtt agatgtttct ccattctctc aggctgaatt
38701 tccattgagc tcactgaaaa cactgaagca atgagaccgt ccacagagcc tccatcatcac
38761 ccccaaccac ctatccggtg ctctgccctc cagcctgttg ctagatgaac tatccatgca
38821 cccattaaag gccaatccct tctctgtgca ccagattcca tccctctctc taactgaaga
38881 accatgtaga gtacttcctc ctcttctcta attcaccaaa ctttcactct ccactggatt
38941 attcccatct gtgaacagat ttgatgtcat tcattccacc ttaacaaaca ctccctggac
39001 ctccatttcc ctgccaggta ttagtatatt tctctgcact tcttatgacc aaaactccta
39061 ggctgggcat ggtgtcagca ctttgggagg ctgaggcagg aggatcactt gaacccagga
39121 gttcaagacc agtctgggca acataaggaa acccctgttt ctacaaaaaa taaaaataaa
39181 aattagccag gcatggtggt gcatgcctat agtcccagct acttgagggg ctgagatgga
39241 aggatcactt gagcctggga ggtcgaggct gcagtgagct gtgattgtac cactgcactc
39301 cagcctgggt gacagagcaa gaccctgtct ccaaaaaaac aaacaaaacc ccacaactcc
39361 tcaaaagagt tgtctctact tactgtctca aattcctttc ctctcaagct aatataaacc
39421 tattccagtc aagcctttcac ccttcccatc ccattaaagc tgttcttgtc aaagtccaca
39481 atgatcctgg tcaatttca acctttatct ttcttgagcc atcaggagca ttttgacctgg
39541 ttgatcattc cctcctgttt gacaaacctc ctacacttgg ctttcagata accactcccc
39601 tagttttcat cccatctccc tggaagtgct cctcagtctc cttcactggt tattccctcg
39661 ctttctcaacc tgttaataat aaaatacccc aaggcttcat ctttcggtctc tttcctttcc
39721 acagccaccc tgtttcgtag ctttcaattt cgttcacata ccgatggctc tcgactgata
39781 tccagtgtca acctctttcg tgtcttcctg ttcactagtc atccgaaaat acaagttcaa
39841 accaatcccc gccagtccct tgaaacacct ctccacctaa ttttctccat ttcatctaat
39901 gataactaca tttttccagt cccttggtca aaaagctttg gtgtcacatt tgatgttgct
39961 gtctgccttt catattccac atctgatctg tcaaaaagtc ttgttgaaat cttcaaatta
40021 tattcagaat ctgaacactt ctcaccacct tcactgctga ctacccgagt ttgagtctca
40081 ataatctctg gcctcattca gtggttccta agttttgctg cacgttggaa taacccagga
40141 tcttttaaac atgctaatgc ctgactccca ccccttgata ttctgattta ataggtgtgg
40201 gatgtaatct gggcactggg aatttttcac tgctctccag gtgatttcaa ttgcagcaaa
40261 gtttgggaat catggcctg gctatggtaa ccgccaccca cctgatctcc cacctccac
40321 accaacccc tcccacagtc tattctcaat gcagcaaata gacatgcttt taaattacag
40381 atcagatcca ttcaattctc tgctaaaaac accagtggct ccccatctca attaggtaa
40441 aagccaaagg cttttcaatg gcccacaagg tgttacatga gctgcactgc ccctgtccc
40501 atgcgccact cctctgacct ctctttcaca ttgcctcacc cactgctccc gtgatgtcag
40561 cctcctcagt ctccttgaac acccagaca tcctctcacc taggactttt tttctttttt
40621 gagatggagt ctcgctctgt caccaggcta gagtgcagtg gtgtgagatc taggctcact
40681 gcaactgcca cctcccaatt ctcctgcctc agcctcccgc gtagctggga gtgcaggcgc
40741 gtgccaccat gcccagctaa tttttgtatt ttcagtagag acagggtttc accatgttgg
40801 ccaggatggt cttgatctct tgaccttgtg atctgcctgc ctcagcctcc caaagtgctg
40861 ggattacagg cgtgagccac tgcgcctgac cttcacctag gacctttgca ctaaccatta
40921 tcttagccag aaatactctt tcccacatat ctacacatca agtattagct caaatatcac
40981 attgKcaata aggcctactg taacccctat ttaaaattat accttaacc acctatctcc
41041 ctcccctctc tgagataaaa cagggaagag gtagaggatg gtgccattag ataaggaaga
41101 gcagatctgg agtaataata gagttctgtt tgggacatgt taagtttgag atgcctatta
41161 gacacccaaa tctaacaaga tatcaaatag gggaaaagtt ggggttggac tggaaacctg
41221 ggagcaaaca cgtggtgctc tggggatcac cttggagaga caaggctgag tgaccccat
41281 ggaacactag tattctgagg tgaggcagag acagagttca caaaagaaag agaagagaaa
41341 ccaagagagt tggagggccc tgtcataaaa gatgttcatg gaggagttga caaaaagagt
41401 caaactctgt aaaatacttg aagagattta ttctgagcca tgattgacca actgaggcaa
41461 gacaggcaag ctccaaaatt ggggctttgc ctgggagggt tcttggcttt gcccaggaaa
41521 caattcaagg gtgagctgat ggtgttaaat agcaacttgc attgaagcag cagtgcacag
41581 ctgcagcaga gggactgctc cttgccgagc agggctactc acaggcagtg cccagaagag
41641 cagctcagag gcagttctgc agtcatatct ataccccatt ttaactgtat tcaaattaag
41701 gggcaattta cgcagaaatg tcaagaatga ggatggtaac ttccaggtca tcaggtcatt
41761 gccatggaaa ggggagggta atgttcaggt gttgccacgg caatagtaaa cgtacatggc
41821 atactggtgg gcatcttatg gaaagttgct tccacccctg ccctgtttca gctagtcctc
41881 aacttgatcc agtgtccaaa ctctgcctcc agaacagagt cccacttcct acctcacatg
41941 gtctgtgaca gagccccagg ggatcctgag aacatgtgtc caaggtggtc aggttacagc

42001 ttgattttat acattttagg gagttataag acattactac atgtaagatg tatattggtt
42061 tggtccagca tggaggaaaa gttaaatatt aaatctgaat tcaattgaac ctggacacaa
42121 acaatagtca ccaagtcctg gaacaagttt tgtgagtccc ttgaggcttt catccagcgc
42181 tgtttcagag aaatctctat ttcaatctat tcctatacat tagttattga aaaacaatag
42241 acaatagcaa aaacaagttg accttttgt gttccttgag cctggttgtg aagggccctt
42301 gtgactgggc ctcatgccaa acaacttgtt acaaaaagag ctagggtccc aggcccagcc
42361 gaagcttcag gagacctatc ctcatctgtg caaggaggag tggccaactc tggagcccag
42421 gctgttgctt cctggtctgg tggtgaatcc tccatagtct ggtgagtgta gtgcccaact
42481 ctggagccca ggatgttgct tcccggtctg gtggtgaatc ctccatagtc tggtgagtgt
42541 agtgtccaag tctggaaccc aggctgttgc ttcttggtct tgtgataaat cctccatagt
42601 ctgatgggtg ggtgtgtgtg tgtgtgtgtg tgtgtgtgtg tgtgtataca catatacttt
42661 cccttctacc cttcccattg caatttgctt attatatctg cattgccatt tacatgggat
42721 aaaggtcgtt tacccttaaa ggtattgtgt atgtgtcttt tcttctcccc tcacgcatat
42781 cccacagaga acaaccagaa aggtgggaca actcaaagca ttgatgtggg gtcagggggc
42841 aacactttca ggtcacaggc agattcagtt ttctctgact ggcaattggt tgaaagagtt
42901 attatctata gacctgaaat gaacagaaag gaatgtctgg gttaagacac agagttgtgg
42961 agactaaggt tttatcatgc agaggaagcc tccaggtagc aggcttcaga gagaatagat
43021 tgtaaatgtt tccttttttt tttttttttt tttgagccgg agtctcactg tgtcgcccag
43081 gctggagtgc agtggtgcaa tctcggctca ctgcaagctc tgcctcccgg gttcacgcca
43141 ttctcctgcc tcagcctccc aagtagctgg gactacaggg gcccaccacc acgcccggct
43201 aatttttgt atttttagtg gagacggggt ttcatcatgt tagccaggat ggtcttgatc
43261 tcctgacctt gtgatccgcc cacctcggcc tcccaaagtg ctgggattac aggcatgagc
43321 caccgcgccc ggccgtaaat gtttcttatc agactttaag agtcggttct gtgctctatc
43381 agccttaagg tctctgtgtt gatgttaaca ctggttagca gctcctgaat tctaaaaagg
43441 aggagggaat aaggaggcat gtccaacccc acttcccatc atggcctgag ctagtttttc
43501 agtttaactt tggaatgccc tgggctgaga attattttcg gtttacagag gagaacttat
43561 gttcattggt ataggatgac aatgaggtca gacaaatacc actgaacttg gcaggctggg
43621 aagttacaaa gcttagcaag gccagtttca gtgtcatagt ggggtcaaag cctcgttgtt
43681 gcctcaattc tagtagggta catattcctg tctttattaa tgggagaggt tcttaatctc
43741 cagcccatgg acaaaggaga tcatagatgg gtttcaggaa aacatcccaa gtcctgcctc
43801 caaattttgc aaaatttgt gcctgtgtat ttttctggag aacgtaaacc aaacagtgtc
43861 tgagacaggt ctcagtctgg aggtttattc tgccaaggtt gaggacacac ccaggaaaaa
43921 gagacataag ttatcatgga atctgtggcc tgtggttttt ccaaagaggg ttttgaggac
43981 ttcaatattt aaagggaaag agcagacaga aggggaaaga ggaacaacta tgcattcatt
44041 tcacactcag taaatctgcc ttttacagaa gacaaagtaa acatagagga aggagtcaaa
44101 tatgcatttt tcttggggtg gactgaaggg tgatttctag tcttgtcctt gtcccctacc
44161 tactgtaaat ttgcatggtc agggtggaat tcaacagaag tgttgtaagg taaagactct
44221 gccactcaca aggaatttcc ctgtgagcaa ctcctctggg aggccaccta gggagatatg
44281 tgggcttctg tctttgcagc tgtttaggaa cagaaggaag gcagtttttg cgtgactcag
44341 ttcacaagct taactttttg ttgttgttgt tgttgttgag acagggtctc gctctgtcgt
44401 ctaggctgga caacagagaa tgatctccac tcactgcaac ctccacttcc gggttcaaga
44461 gattctcctg ccttagcctc ccaagtagct gggattacag gcgtgcacca ccacgcctgg
44521 ctaatttttg tatttttagt agagacaggg tttcaccatg ttgaccaggg tggtcttgaa
44581 tgccagacct cagatgatct gctggccttg gcctcctgag atgggcatag tgctagtatt
44641 acatgtgtga gccactgcgc ccggccctaa gcttaacttt tttctttggc agagtttagg
44701 gtcccgagat gttattttcc ttccacaaga gacatccaca gctttcacga tggttaccga
44761 tcatatgtgc cattcatcta agaccaaggt gaccacctgg tcccaaagcc tgcacctcgg
44821 attcttactc gattcccgcc tggtctcttc caggccctca gttagtttcc acaacatggg
44881 agggttcctc ctccgtggtc tcgcccattc gcgttcccac ccaccctccc cggatgtgac
44941 gaccctgggc tcccactccc ccccatgaga gaccatccac ttccaccctt tcacttaggc
45001 ttcctggcgc agcctctatc caggaactct gtcccatagc tgtactgccc aggtcgagct
45061 ttctaacccc aagatgccac tccgttcaga cgttcccatc ctccatccct gagacccggg
45121 gcaggatcgc agcctagggg cctcacRggc cgcctgctac cctgttagtt gcaacacggg
45181 gcggggcgtg gctttgtgca cgtcggcttc cgggaagagc tttacgatac attgaccgac
45241 attttacgac aggcgggatt gttttgtggc tgtcagcttt cYccgtggtc tgagtttgtg
45301 gctgcatttt tatctctggt ggctctgcta cggcggcgca gaaatgaggc agaagcggaa
45361 aggtgcgaaa ggggaaggag atgggggaaa ggggtggtcc gaaaggggcg aacgcccagg
45421 caatcaaatg ctgaaccgaa cttttaccgc gagaatccgc tacccagtcc agtcgccccg
45481 ccacctaggg tcagtgtgtc cattctggtc cccgagcctt ctcgtttttc ctgttttgct
45541 ttttgaagca ccctaccctt cctctcttcc tctttggcag tcacgtggtg tcttgtttga
45601 atggcaggga aaccattatt ccaatatatg ccctccgagg agttaacgtc gatttaacgg
45661 gttgtaggac ttttcatttg ttaagatttg tttcacgaca catttgacgt gttagagagt
45721 ttcttttaaa gccttatttt aagatattaa aaaaacctta attatccttg gattcagtgt
45781 aagagttgtg catgcaatta ttcccatttt tattacatca tgagttagca atgaacaatt

45841 ccacctttgg tttttcaaca ggacggattc aaatttgaaa tattctctca caggttctgt
45901 tcctatttct gtatctcaca ggttctgttc ctatttcatt tgaccagctg gtctaatcat
45961 ggtaattgtt gtcagaataa tagctaccat ttattgagct tgtattttga agtcggtatc
46021 atttccattt tacagatgaa gaagctgaga ttcaaagagt taagtaactt tcccagacca
46081 aaattatact tagatatgga gctggctggt caggctgtat ctgtgacctc aaaaaacata
46141 aaatgaaaaa taaatacatc gttaatcMct atgcttcttg acattaactg ttatttttct
46201 ttcttccaag caacaattct aagtgtccaa gttaccttag attaagtctt gtcatatttg
46261 catgccctaa attaatttgt tatctcactc taacttgctc cttctcaatc taccaggatt
46321 cttttagYtt cttctgtcac caagtcatgt tgattcttac ttagaaatta cttcttgata
46381 tagtttattc ctcttcattc tggccgccaa cctcctaacc caccttcatc actaactaat
46441 atttgaatgg tatttcagct ttcatataca ttatttattt gagtcttaga atggttttgt
46501 gaaatttgga tgtattaccc caattttaca gacaaggaaa tgggcactca aaagttgttg
46561 atcttggcca ggcgcggtgg ctcatgccgg taatcccagc actttgggag gccaaggcgg
46621 gtggatcact tgaggtcagg aattggagac cagcctgacc aacgtggtga aaccctgtct
46681 ctactaaaaa cacaaaaatt agccgggcgt ggtggcaggt gcctgtaatc taatcccagc
46741 tacttgggag gctgaggctg aggctgaggc agaggcggga gaatcacttg aacctgggag
46801 gtggaggttg cagtgagccg agatcgcacc actgcactcc agcctgggtg accgagcaag
46861 actctgtctc aaaaagaaaa agaaaaagaa aaaaaattgt cgatcttttc cgttaccaca
46921 cagccagtag gcattgggac tggatcctgt cttagatttt gtgggttttt taaaacaatg
46981 ttgcctttca agagccattt gagtagtatc catattatat gtattctttt tcactttctg
47041 aatcattctt tgtaccgata atattcttac cttccttaaa cgttactttc aactttttat
47101 ttccaaagtt gagaatatgc aattcttcac tgtctgttgc attccatttc aatgcctttg
47161 cctagtggcc agggtcccct gtaatctgtt ctttattaca ccctgttaga aagctggatt
47221 ttagttaggc tgtgctgttt cacacaaaga taggtaattc ctatgcctga cattatttct
47281 tctggattgc cttctgtttt gcatgtccaa atcttgccct atctttaaag atccctgtgc
47341 catttccttc atgaagtctt ttcctactca tttactcttc cagttcttga tacactcaag
47401 agctatacaa gtggtttcca aatcttatct gttcttatca gccgatcccc ttttaccctc
47461 caaataaatt cttacacaga acctcaatat ataaacagct gaaagcagag ctgctgtggt
47521 ggaaataaag agacctcctc cttttttttcc tccatgcctt attttcctct tcccttctcc
47581 cttcctctgc catgaccacc accagtccta cctctgttgc atggccccctg aggcaccttt
47641 gtagaactct ggaagtgctg agttacatgg tttggaaagc atttagcctt tgagtataga
47701 tggactttat ttctctcaaa aattgttgtg tatatgttag ccttgcctca ttaaattaga
47761 tgcagtgtgt tacagtgaaa aaagcatgga agttgtggtg aaaagagctg gatttgagtc
47821 ttggctctgc tgtttacgat agcttgttaa cttgccttag cctcattttt cacatctata
47881 aaatgggata acagtaccta ccctccgtgt tactgtaagg gttcaaatga gataaagtaa
47941 atgtgtgggc tccataattg ccagggcctt ccatccacgc tttcattatg ttttagcttt
48001 ctctgcagtg tgagtcctca gccccctggg ccacggacca gtaccggttc atggcctgtt
48061 aggagctgag ccagacagaa gaaggtgagc agcaggcgag caagtgaagc ttcatcagta
48121 tttgcagcca cttcccatca ctcatgttac tgcctaagct ctgcctcctg tcacatcagc
48181 agtggcatta gattctcaaa ggagtctgaa ccctgttgtg aaccgtgcat gtggtgggtc
48241 taggttgtgt gctccttatg agaatctaat gcctgatgat ctgtcactgt ctcccatcac
48301 ccccagatgg gagtgtctag ttgcaggaaa acaagctcag ggttcccact gattctatgg
48361 gaacagaatt cgttatggtg aattgtataa ttatttcatt acatataaca atgcagtaat
48421 aaaaataaag tgcacaataa atgtaatgca cttgaatcat cctaaaacca ccctgctccc
48481 ctggtctgtg gaaaaatcat cttccataaa accagttcct tttatcaaaa aggttgggaa
48541 ccactgctct acaggtgaga agcttgcttg ctgacagctt ccaagctgat atcccacagc
48601 ttttgtccct ggaaaaagac tggcattttt taccttgaag aaaagagctc agattggcct
48661 ggcttagaga tatgcccatc cttgaaccaa tccttgaact gtgcttgagt ggatggcgtc
48721 atacaagaac ctgtcagctt ctgctgttgc ctttggatga gaccgagagc cccagttgcc
48781 agaagttcat gatggtggac agacaatatt ttagaaatgc attaagattc ttaggcagat
48841 acctgggttt gagtttcaac tttactcctt gatagcatct tcatgtaaca ggcacatatt
48901 cttgttctgt ctacctctgt tctgagaatt acctgaattc atgcatctaa atgttcttta
48961 tgaactctaa agtattatgc acatattagt aattacacct ctggagataa agggaagaga
49021 attactttgg tcctttcctg tgtgattaag ttctttctcc tcacattgtt tctactYctg
49081 tatcctttcc tgtatttatt tttaataatc tcatagagta tgtgcttcta aagggagctt
49141 ttcccatata tatgtaaagc cacgtttgtt ttaaagatac aaaagatatg atcaaattgt
49201 aaacagtaga gatttagcat cttctgaact tgagctattc atttggcata tttgtatggt
49261 ttcggatgga aaactgctac taaatcagat tttaaaatct tgattgaatg atacgatttt
49321 tgacattgtt gaatattaac tttccaggag atctcagccc tgctgagctg atgatgctga
49381 ctataggaga tgttattaaa caactgattg aagcccacga gcaggggaaa gacatcgatc
49441 taaataagta agtggatata aagagagagc aagcttgttc ttaggtagca gatctctttt
49501 atgaaattat ctagtactac ttgttttcca gctcaagttt tattttagtt gagaatttta
49561 gctttctgcc ttgccttgtc attcatttct ttttttttt ttgcaagttc cgcctctggg
49621 gttaacgcca ttctcctgcc tcagcctcct gagtagctgg gactacaggc gcccgccacc

```
49681   acgcctggct aatttttttgt atttttagta gagacggggt ttcaccgtgt tagccaggac
49741   ggtctcgatc tcctgacctc gtgatctgcc cacctcggcc tcccaaagtg ctgggattac
49801   aggcgtgagt caccgcaccc ggccgtcatt catttcttga tggcaaaatt gtctcagctt
49861   aagaatacta atagcttcta acatttattg ggcacttact gtattccaga cactgttgct
49921   aatgcattgt atgtattagc tcagttaatc ccctcaaaat tctgtgagat aggtactgat
49981   accagccaca cttgacaggt gggtaatctg agtcagagag cagttaaata atttgtccag
50041   gggtaagtaa ctagtaattg gcagagctgg gatttggaat taggtcagcc gtctccagag
50101   cccatgttct tctgtgctgc atcgctgcac atcctacttt ccttccctac tgtctccagt
50161   gaagcagcag ctttctgtca ggaaaaccct ccctttgggg cccctgatct aatccaaccc
50221   tcccctgctg tagaacctct ttgacacatt catccacttc ctctccataa tcatttttag
50281   cttggacttt cctacagtct caaataagag ttgtctttca tctctgcatc tatttttttt
50341   ttcaaactat aatatatatt cactctatgt agatctttcc taatgaaagg gttctctccc
50401   caaccccagg tcgtctaatc atcacataca ggaatgacct tttcttagac tctcttctct
50461   gatacttgag atgctgcaat attttacccc ttccttgaat cctcatgctt agtaaatatt
50521   tgctacagga ataagtaaat atcctctttt gactataaag ttattgtatt ttactgattt
50581   ttctaccggg tctttagaag tttttctttc ttttttgctt ggtctatccc ctgatctatc
50641   aaatctttaa tttctagtga acatttctac atcttataata tatttgttgt tctctttaat
50701   ttagcacatc taaagctaaa gctgccatcg tccttaaaac tcgcccctcc tcagatgtca
50761   ccagcctatt actggaaggt ctctcagtct ggcttcaacc tgcttttcca agttttaaaa
50821   cctctgtacc tttacattga aaatcttctg ctttctgtca agttggtctg cttgtatttc
50881   ttaaaatata tgcattcctg tttttgcatc tgcacataaa tcagcctgtc tgccctccat
50941   gtcatctttg tgtctttagt gactgagacc tactcttttct tctgtgctca tttccatgaa
51001   tatctcccca gcacacatca gattcctccc tgaactctgg aagcattcat tgttggtatg
51061   tgtgtgtgtt ttatgacata tgttttaatc atttatacat taattttctt ggtacgcctg
51121   tctgcaaaca tgtaaacata gaacatgaaa ggactgtgcc ttgcacattt gaacatagca
51181   ggtattcagg cagcctcttg tacggtgtag gtcctcagtt aatatttgtt gacaaatatg
51241   tgagcacttc acagatattt ctagatggat taaagttaga agacaggggtg actgttaaga
51301   gtttggctag gaggcacaaa gaaaagctgg taaaagtttt ttttaaactt tcaaaaatat
51361   gtacttttatt tcctatttgg ttctgcatag ccatccttga ttttttttttt aattgttgtt
51421   gttgttttgt ctaagacagt agttgtcaac cagggtgat ttcctcctca ggacatttgg
51481   caatgtctag ggacatttttt gagtgttaca acaggaagac aagaagaagg ctggtagtac
51541   atagagacca aggatgctgc taaacatccc tcaattcgct ggccacctgc cacagcaaag
51601   aactgtgtgg tcccaaacat cagtagtgct gaggttgaga aaggtggagt cagaatagtc
51661   ctttgaagct gcagcactat tctgaactag atctatattg tgtcatcgtc cagggaccct
51721   tctccctcca tagtcctctg gttttctttc tggtactcaa gggtgggaag tagtcattca
51781   ctcgtgaatt ttattcttct atttccctga tagtcacaga tcttaaaact atccttgtca
51841   cgtggtgaag ggattggaga gtgacagttg ttaatgatgt tgtttataga tcatcctctt
51901   ggtagcttgt ccttaaatca ccgtRatctt gataatgtga gatgcttcac tttcagggtg
51961   aaaaccaaga cagctgccaa atatggcctt tctgcccagc cccgcctggt ggatatctat
52021   gctgccgtcc ctcctcagta tcgcaaggtc ttgatgccca agttaaaggc gaaacccatc
52081   agaactgcta gtggggtgag tgattcgact catgaggtat cgacacactg ggtatctgtt
52141   Ytggcagaag tccctgctcc atgtgacRcc cgtgtagtga ggtagaggtt ggggattctg
52201   aactaatgaa gtccctgtat taggatatgt gctggagtgg agacctgtgc tgaatgcaag
52261   gagagcagag agagaaaaaa atataattgt gattaaagga gtagatgatg tttgacctc
52321   tttaaaaata tagatttagg cttggtgaca atcataacag gataaatgtt ggccatctta
52381   agctggtagc tttcaatata attgatgctt atgaaaggta cttttgaaag gtagttaatg
52441   gtgcaaagta gttctgtata tggtgattat gagcactgtg gaagtccaga caacagcgat
52501   gtccctgcag caaaaggggc tggggaaggc ccagtagaaa gcacacagct tgcttgaccc
52561   atcaagccaag aagagcaggc tctaagtgtc atgggagcaa ggacacagcg gctaaggcac
52621   agaggtagaa atgacaggaa ggcgctggtg cacgcaggaa atagcgagta cgccagacctg
52681   aagggtgtta acagttcagg agagtaggac tgtgcgttga acaggtagtt tgggatcagc
52741   ttgtaaaaat cttaagtgtc tggcaaagca gctagataat aggaaacaaa agttttgaaa
52801   aaggtagtaa tatgaacaaa gtagattttc agaaaattaa tttggataca acatgcaggg
52861   tagtttggag acaaaaagac tagcttagat gctctttggta tgatgtcagt atgcagtgtt
52921   aaggacttga gttaggatgg agactctagg atgaaaaaag atgagtgtga gatacatgca
52981   cagaaattga tagaattaag accctcctac catatggtcc ccagcaccaa attctgttcc
53041   taatgtgatc ccacaagttc attctgttat ttgaattggg atattatatt ccaggcagct
53101   tgtgttgact tggtgaccat atctcctgga tcaccttacg tttgtggcta attaaaccct
53161   aaaatttttta catacaatgt accaccaaac ctcatatcct cttctttgta cttaagtgtt
53221   tttgttttgt tttgtttgtt tgtatctagt tgtaaagact tgttagccag gcacggtggc
53281   tcacgcctgt aatcccagca ctttgggagg ccgaggtggg ccgatcacaa ggtcaggtca
53341   agaccatcct ggctaacacg acgaaagccc atctctacta aaaatacaaa aaaaaaaaat
53401   tagccggcgc ttgtggcggg ggcctgtagt cccagctact ccgaggctg aggcaggaga
53461   atggtgtgaa cccgggaggt ggagcttgca gtgagctgag atcatgccac tgcactccag
```

53521 cctgggcgaa aaagcgagac tccatctcaa aacaaaaaac aaaaaaactt gttaagaaaa
53581 actaatagtc catgcccctc acctcccttt ttctacccta gggcaaccat ttttaactct
53641 tagccaattt ctttagcatt aacttccata tccataaata aaataacatt ctttacataa
53701 tagataagtc ttgactttct ttttttttt ttttacctga gacagtcttg ttctgttgcc
53761 caggcaggag tacagtggta cgatcttggc tcactgcaac ttctgcctcc cagggtcaag
53821 cgattcttgt gcctcagcct ccaaggagac tgggattaca ggcatgtgcc acaatgccca
53881 gctaatttt gtattttcag tagagacagg gtttcactat gttggccagg ctggtctcga
53941 actcttgacc tgaggtgatc tgcccgcctc agcctcccaa agtgctggga ttacagacgt
54001 gagccactgt gcctggccga ctttttagag ttaagcatta tgtgtgggct tgccattaaa
54061 gaagacagaa acttagcaac ctttcagcct gactggcaaa ccgaggcttc tgtgatacca
54121 ccctctctgt ttcttcctct gtctctgatc atttctgtcc tatcttggct accttattgt
54181 gcttacctct aaaagttgat gttttctgtt gtcctgggct cattgtgttt ggtattttac
54241 atgcttttctt tggtaacctc atccatttga tgattttagt attgatgtat gctgactccc
54301 agcatgaacc attccctgag ctccagactc ctgtcagatt gtcagttagg cactctgtcct
54361 ttgactgcct gagaacctcc tgaagtatag cataaccaaa actaatacca gacttgctta
54421 ttcacctttc ctgtccatgt tagttcatgg taccaccgtg cactcagttt ccaaaaaatg
54481 tgaaatgcat tttccgttcc tactgccact ggtaagaatg ctttggcctt tattatttct
54541 tgtttagatt atttcagtca tttccttacg catctatttt gtcctaccta catgaaatgc
54601 atctttaaca gtgtcacaag agtgatctat tgaaagtatc agaaacacac agctggtggc
54661 cattccctat ctactgccat tctcacctcc atgcttttat tcttgctgtt tttctgatgg
54721 tgctttgttt atttataca gtagttttag gtttatagag aaaaaaaatt tatacacttc
54781 ctctagcacc ttcacccctа ccccagtttc cctattatta atatcttgca ttgtttggta
54841 catttgttag aattgatgaa ccaatattgt tgcattatta ttaaccaaag cctgtacata
54901 cattagaata cactctgtgt tctacatttct gtaggttttg ccaatgcata atgtcatgta
54961 tccactatta ctgtgtcata tgaaatagtt tcactaccct aaaatctcct atttgtggcc
55021 gggcgcagtg gcttatgcct gtaatcctag cacttgggga ggctgaggca ggcagatcag
55081 ctgaagccag gagtttgaga ccagcctggc caacatggtg aaaccctgtc tctactaaaa
55141 atacaaaaat tagccgggca tggtggcggg cgcctgtaat cccagctact tgggaggctg
55201 aggcaggaga atagtttgaa cccaggaggc agaggttgcg ttgagccgag ataatgccat
55261 tgcactccag cctgggtgac agagcgagat tctgtctcaa aaaaacaaac aaacaaacaa
55321 acaaacaaaa acagctccta tttgtccctt tccctctgca tgttctagac gtaacctgac
55381 ttccactgat tgttttattg tctttaataa agtttgcttt ttccagagtg tcatgtacag
55441 taattggaat catacagcct ttccacttag caatatgcat tgaagtctgc catgtctttt
55501 tgtgacttgg tagtcattc ttttttttta attactgaat gatatccatt tgtacggatg
55561 taccactatt tgcttattca ttcacctatt gaaggacatc ttggttgctt ccaatttttg
55621 gcagtttaa acaaagctct gtgaagggtta ttgtgtccac ctacatttcc agcttcactg
55681 agtaactgtc aacaagtgca actggtagat catatagtaa gactatgttt cactttgtaa
55741 aaaactgcaa actcttccag catggctgca ccattttgca ttcccaccag cagtgagtga
55801 gcactctgat gttccacatc cttgctaaca cttggagatg tcggtgtttt ggatttтatt
55861 taattaattt atttatttta agacagggtt ttgtcctgtc actgaggcta gagtgtggtg
55921 gcatgatcac agctcactgc agcaacctcc caggttcaag ctatcctccc acctcagcct
55981 cccaagtaac tgggacaaca ggcatgcacc accacaccag ctaatttttg tgtttttttgt
56041 agagacaggg tttcaccatg ttacctagga tggtcttgag ctcctaggct caagggatcc
56101 tcccagcttg gtctcccaaa gtgctgtgat tataggcgtg agctatggtg cccagccagt
56161 gttttggatt ttagccattc tcatagttga acagtggtat ctccttgttg tttagtttgt
56221 aattccctaa tgacatgatg ttgagcatct ttccgtatac ttatttgcca ctgtatatct
56281 tctttattga gatatctagt cacatctttt gccctgttct taatttgggtg ttttcttact
56341 aggttttagg agttctttgt atatcttagc tggaaatggt ttatcaggta ccaatttatgc
56401 agatattttc tcctagtctg tggcttgtct tttcattgtc tttctcagag cacaacttтt
56461 aaatatagac aattaggtcc ataacccatt ctgagtttgt atttgagttc gtgtttgtgt
56521 tcttgaaaca ccatggttgt taacttggat acattactgt catctaagcc tcagacctca
56581 cttaagtttc accagccgtt tcaataacat ccacacagaac ctagtttcaga atcacctgtt
56641 gcatttaatt gtcatatatc tttagtctgg acatttcctt tgtctttttt ggactccgtt
56701 atcttaacgc ttttgaagat ttctggcaag ttattttgta gcacgtccct cagtgtgggt
56761 tcatcagctg ttttctcatc atgagattca ggttacgcgt ctttggcccg tgcctcatag
56821 aagcagcact acgttcttct cgtcatctcc catccagtgg tgcgcaggtt tggttttcct
56881 atcactgatg ttcctcattt tgatcaaggt gctgtccacc agacttaccc tctgtcaagt
56941 tatttttttc cacttttgtat taagaagtgt tgtatggaga aatactgaga aactaggtgg
57001 atatcctgtt tctcatcacg taccccagttc actcctttat ttgtgtgaag gaattaatgg
57061 tttcctattt ggtgggttat catctgttac tatttatttt gatgcacaaa ttatttgtgga
57121 cttgaccagt gggagccttt tcaagctgat ttctatgtct ttttaaaatg tcctcatcat
57181 tctttgagca gtttctagct ttctagcaca ataaaatgtt ccaggcttgg ccagacatgg
57241 tggctcacgc ctgtaatccc agcactttgg aaggacgagg tgggtggatc acctgaggtc
57301 aggagtttga gatcagcctg gccaacatgg caaaaccctg tctctactaa aaaaaaaaaa

```
57361  tacaaaaaat tagccaggca tggtggcaca tgcctgtaat cccagctact tgggaggctg
57421  aggcaggaga atgcttgaa cccaggaggt ggaggttgca gtgagccaag atcacgccat
57481  tgcactccag cctgggcaac acagtgagac tccgtctcaa aaaggaaaaa aaaggaaaat
57541  gttccaggct tatcttagac tttcttttgct ccagccctgg aatcagccat ttcccaagg
57601  agccctggtt tcttttagtt ggagaaggat atttagatac taagacctgg gtcctaggtg
57661  tgcttactgc tgttagggtg ttgctgctgc cagactctct cagtggacca agcgaggaca
57721  tatatatgta tagctgcata cataacatgc acacatacat gtaacacatt tccatttgta
57781  tttatttatc agtctaccat atgttgaaca ctctgattgg ccacaatacc tttaattcca
57841  cccagcccac agagttcatt ctgcttctct ctctttccat gtttatagct acttctctga
57901  tagtaagaag cctggcttgc tttcactttt gtaaatggcc agattgacc aagtgccctg
57961  gatgtaacca atcttgcgtc tctgccactg cctcctgtcg tcacctcact gaggctctgt
58021  cagacccctc tgaggttatt tacacccaga ccctgaaaca tgaagctgct agtttaatag
58081  tacctgctgc aaatattgag atccagtgtg ttcatgaggc gtttgagtca caaaggttag
58141  gtttatatat aatttctatg aattgcttaa agaaatttct ttcttacagg ctgtttacta
58201  agacaatcag agagagaaag actaagaatc actttggctt taacagttaa ttttgtattt
58261  tgtacttaat ttattgtaaa atggaatata acttcacata tatattacat acggacaatt
58321  taaagatgat taatattgaa cagagatcac tcttgtaccc attgccagc tcaagaaata
58381  cagcctcggc cgggcgcggt ggctcacgcc tgtaatccca gcactttggg aggccgaggc
58441  gggcggatca cgaggtcagg agatcgagac catccccggct aaaacggtga accccgtct
58501  ctactaaaaa tacaaaaaat tagccgggcg tagtggcggg cgcctgtagt cccagctacc
58561  tgggaggctg aggcaggaga atggcgtgaa cccgggaggc ggagcttgca gtgagccgag
58621  atcccgccac tgcactccag cctgggcgac agagcgagac tccgtctcaa aaaaaaaaaa
58681  aaaaaaaaaa aaaaaagaaa tacagcctcg tcaatacctt tgaagcccct ttttgccact
58741  ctctggttgc attcctctcc ttccttccga gggataagca ctctgtggag ttttatatta
58801  attatcctat aatagcttt ttattcatct ttctttata gattgctgtc gtggctgtga
58861  tgtgcaaacc ccacagatgt ccacacatca gttttacagg aaatatatgt gtgtaagtat
58921  ggtgatttta ttaaattgta tgtatgtttt aattaagcta aatatgcccc ctctagccct
58981  tagtcagtac atcctggtaa tgtttaaaac ttcagcttaa tagatttata gattactcct
59041  ttcaaacaag caaccattgg tagatatttt agtgctttaa aattggaata tataaggccg
59101  ggcaaagtgg cttacgcctа taatcccagc attttgggag gctgaggcag gtggatcacc
59161  tgaggtcagg agttaagacg agcctggcca gcactgtgag actccgtctc tactaaaaat
59221  acaaaaatta gccgagcgtg gtggcatgcg ctctagtcc cagctactta ggaggctgag
59281  gcaggagaat cgtttaaacc tgggaggtgg aggttgcagt gagccgagat cacgccactg
59341  cactccagcc tgggcaacag agtgagactc catatcaaaa taaataaata aaattagaac
59401  atatgaatat tttaatttat tgcaatatac aattctaaaa atgtaggtta tggaactcac
59461  aacagtagac attgggatat gcaactcaaa acagcacatt ctgttaaact cataaatgaa
59521  acatgggaat atgagctgcc taaattccac gtcagaaatt taaaatgaat ttggatcaga
59581  aacatatcaa aataaaaaat tatccttata cgtaaccttt agatttctca aactcaccta
59641  tttgaaagaa ttagcggaag agtttgcatg attctgggta ggaagataaa aggggggaaa
59701  gattttcttg agtgtggttc ccaagagaac actgagtatt gattcaaact taggaaaact
59761  tcatttctgt tatttgcccc taaaagctta aacctctgaa ataaacacaa ctgcagttat
59821  tttgaaaatg ggtgtaataa tgtcccttta catatttatc ttatttactt cttggtagaa
59881  aatacattat ttacagatac tgcaaaggta gattcttctg ttaggatttg aaaaggaagc
59941  tcatttgtta tcaggattct ttggagatgg tagatgcttg gaactagctg attgaactca
60001  gttttgcatc tgacatttct gttcttttgt tgtactggca gatactgccc tggtggacct
60061  gattctgatt ttgagtattc cacccagtct tacactggct atgaggtaca gtaactttga
60121  ggctgtcctg atgaaatgtt gcatcatgct ttacctgtag tatggttta cagtactgg
60181  ctttctgaca attttttgtt tttgtttttg ttttttctg atttaaaag ctgttcattc
60241  accaaatatt tgccagtgtc tactagtgcc ctatattatt ctagccacta gagaaatact
60301  tacataagca taaataatac ttacttctta tcccaaatgc tgttctaagt gctttacaac
60361  tgtaaacctt attgcagtgt tttgaagata gacactatca tgatcccagt ttgccaatca
60421  ggaaactagg gcatagcagg cttaaacagc tggcccaaag acacactatt agtaagtgac
60481  aaccaggttt cgaagtctgt gctgcttacc actacattgt actgtcactt tagcagtgga
60541  aaatggacag ggtcccattg tcttctggaa tttacatttt tttttctttt ttttttttt
60601  ttttgagatg gagtctcact ctgttaccca ggctagagtg cagtggcacg atctccttca
60661  ctgcaacctc cacctcctgg gttcaagtga ttctcctgcc tcagcctccc gagtagctgg
60721  gactacaggc aagcaccacc acgcccagct aatttttgta tttttagtag agacaaggtt
60781  tcatcatgtt ggccagcctg gtctcgaact gctgacctta agtgatccgc ctgccttggc
60841  ttcccaaaat gYtgggatta caaggcgtag ccactgtacc cagcctggaa tttatatttt
60901  aataatggaa ggtagacagt aaagaaacaa gaaaaagtat caggcactca aaaaatgcta
60961  agcagagatg taaaatcaag taaggtgatg gcagctgaga tggttagct gtggtcgtta
61021  gtgaagggatt ctgtgaagtg agattgaagt tgagtctgaa tgacaagaag gacctagtcc
61081  taagaatatg tgaaaggggc attcctagca gagaagtcac tagaatgagg cccaaggaag
61141  gaaagacatg ggggtgttgt gcagtgcagg gggtgaggga agcatgaggc tgggagtgca
```

```
61201  aatgagctgg ggtttgtaag caaaggtaag gagtttccat tttagcgtag gagtcatgag
61261  aagctattag gatttaaggc aggggaatga tacaatccaa tttaggtttt ttgaaagatc
61321  attttgatgg ccatgtagag aaaggggttag agtggagacc agaaagaagg cagaaggcca
61381  gtgaggtgct tttgaaggag tcacccctcct cagaacacct cagaagccag gaaagcttgt
61441  gacttttttc tcatatctgt tttcattttt tttcttgttt tctagggttc aaatttttta
61501  aaatacaaga ggaatgattt cgtgaaaagg cttcctctca ttcctatccc ctagccactc
61561  tttttcactc ttccccctac cagttagtgt tgtttgttat ttcctcccca tccttcaggg
61621  atattttagg gaacacagca tacacaggtt gcctatccct tatgtgaaat gcctgggacc
61681  agaagtgttt cggatttgg attttttctgg attttggaat atttgcatat acatagtgag
61741  aaatcttgag agtggaaccc gaatctgaac atgagattca ttttgggttt atgcatacct
61801  gatacaccta ggctgaatta attttataca atatttttaa taattttgtg cgtgaaacaa
61861  agtttgtgtt aagtactatg tgtggaattt tccagttatg gcatcatgtt ggcactcaaa
61921  aaattatgag gtttggagca tttttgattt ttggattagg gatgctcaac ctggacgtat
61981  tctttatttg actgattcca tataaggtag catatcagag tcctctttca ctttgccttt
62041  tatttacaa tatcttagtg aacatttat gtcagtacat tgttcgtgg ctgtgagtta
62101  ttccactgta tggtggtagc cattacaaac tgtgtggtat tttagaagct tacttaaaag
62161  ttacttatt atatgattct ggtatatgta tgcacatcta tgtctgtgag cagaacactt
62221  tggtgaccct gggattccag aagtgtttat acaaaagaca gatgtgatcc aaggagacac
62281  cctgctgttg aggtgtttat gacagcgtga gtggacacct gccagatgcg attcaggaca
62341  ttattttgaa ccctgacaag actgagaaaa attaatgcgg gtacaagcca cgttttcagt
62401  gttcggaacc atggagagtt ttttttaaaa tacagtcctt ttgaaactac tttttagttt
62461  taattcaRtg tgggcataac aatatttttc tcttctagcc aacctccatg agagctatcc
62521  gtgccagata tgaccctttc ctacagacaa gacaccgaat agaacaggta catttttaaa
62581  aaacatgttt cttaaaaatt aggtgtttat acttagtaag aaqccattgt tgcttgattc
62641  aaattgaacc tgaaataaga atgaaaaagg tgtttttcct ctttgtaagt ttttcaatatc
62701  catttgaggg aggagaaatt tgccatgcct agcaaggtca aaaacactac ttttcttaaa
62761  gactgtattt attgtttaag ggttttatat tctctaagtt tttttgaatt tgtagaaagt
62821  catttgtagt atgaaatttg tggaataaag atgtatgaaa gttcttagac aatgggtggg
62881  tgtgttgact tttaatttcc aaaagtcaga ttaagaagta ttttgactgg ccatgcgcaa
62941  tggctcatgc ctgtaatccc aaccctttgg aaggctgtga cagcaggtca cttgagccta
63001  agagttcgag accagcctgg gcaacatagc aaaaccccat ctacaaaaaa tacaaaaatt
63061  agcatggcat tgtggtgtgc acctgaagtc ttagctactt ggaaggctga ggtggaagga
63121  tccetgagc ctggaaggtc aaggctgcag tgagctgtga tcataccact gcacttcagc
63181  ctgggtgaca cagcaagaac ctgtctcaaa aagaagtatt gtgacagatt tgttgggtgg
63241  aaataggaaa tttcctacaa aggagtacaa agaactagtc ggggtatggc attgttctct
63301  atcatggtca tggtggtggt tacataactc taaatatcta tcagctctca tccattgtac
63361  acttaaagtt agtggatttt atcgtattta aattatacct cagtatggtt gactaaaaac
63421  aagtactatg tacatgacct tgcagtgttc aagaaatctg aacattaata cagatttcct
63481  ttatttacaa gtttatttta aacttgtcca atttaaaaaa tgtaaagcac tgtccatagt
63541  tgtaatagta atgtatagta ggcacatcca agtctaaagt agataatggt acataaccat
63601  agtggataag ttgtctctgg gtttgtttat tggcttattg gtgatactg ttcagtttta
63661  atatccacctt tgctgtcacc caagcgtatg aggaacagga ttgtcggtga caggagagga
63721  ctccatctgg gggagcccac atttttccaa acagtgggtt ctaaactgac ctttgcttca
63781  atttcttttt gggctatgat agttaattta tttaaaatgt aaaactattg agcatgaaat
63841  gcttatgttt accaaaaaaa ggagcatagt ttacaagatt tagaaatgaa catagagcag
63901  tgattctttt cttaaatgca ctagaattac ctgagtaact tctccaaaac gtgtcacatc
63961  ttcacctcgg gaggttctga ttaagtctgc tttaaggtcc tagcaagata tttttaaaaa
64021  ctaccagggt aatttgatg agtatctctt gtaaagaacc atagatacag aaatagagta
64081  ttcttttagt gttgatatat atgtacacac atgcatatat atagtttttc tgtatacgtt
64141  ttttgccatt ttcagaaatt agtgttaatt tcaatacctа tttttaaaaa ttagaatctt
64201  ggcttattgt agtcaacaaa atgaaagatt tgtatcattc tctccactag tagaggagac
64261  ctaattttat tattattatt ttttttttt taaacagagt gtcactcttg ttgcccaggc
64321  tggagtgcag tggcacaatc ttgggtcact gcaacctccg cctcctggtt caagcgattc
64381  tcttgcctca gcctccagag tagctgggat tacggcatgt ctggctaatt tttatatttt
64441  tagtagagac ggggtttcac catgttggcc aggctggtct cgaactcctg acctcaggtg
64501  atctgccagc ctggtcctcc taagtgctgg gattacaggc atcagccacc gcacctggcc
64561  tgaatatttc atttttaatc agactttcac ttttttttag aaagcagact tgaagtgcct
64621  cctgtgcctg gaatcatcca tcaatttag actgctgtct tgatttttct ttccaatcta
64681  ttctttttt cttccattac atcaaatcct tattatgtta catcatcatt catgtatcat
64741  tgttgaccat aaatgccacc ttttgtcct ctaggcttac caccaagtct gacataaaat
64801  acatgatcaa taaatactta ctgttttgca aattgtatta tatttgtctt tactgctttc
64861  tagtttatat tcttcgtgtt tttaaatttc cgctttgtag gtattcaagt caagcctctt
64921  atttgttatt ttatattctc attctccctc cttatttgag ttgtactcac tttttctttt
64981  cagacttggg cctatttttt atccacagaa ttagctaagt gtgtttcatt acttctgatt
```

65041 tttaaactgt actgatgaaa acactgcaaa ataagagatt tgcaatgcct tcttagagta
65101 gttccttatg cttatatcat tctaatgctg atgaattctg ctttcagtta aaacaacttg
65161 gtcatagtgt ggataaagtg gagtttattg tgatgggtgg aacgttatg gccccttccag
65221 aagaatacag agattatttt attcgaaatt tacatgatgc cttatcagga catacttcca
65281 acaatattta cgaggcagtc aagtaagaaa ttcttatttt atcatagtct ccagagtggt
65341 tgtcagttta tgctcctagc agtagtctac gagaatgcct tctgccctgc atccacattc
65401 ttacttctca taatctttct tgtttcatgg gaaaggatta tttcagtgaa aataatgctt
65461 tcgctgaaat aatcttttcc agtgaaaata atccttttac tgaaataatc cttttaaaga
65521 aaaaatgaat acagtttgtt gacatagtag tattctcaaa tagagagatt cKccaaatat
65581 ggtccatgaa tgtctttcca gcccacccaa gaaggggtgt gggagtattt tagctgctgt
65641 aaaatcagca aaacaaggta ctgttattta aaaacctaat ttatagtaaa tatttcataa
65701 ttattaaata gtaactgttt atgattggga tcttagtctg tgttgtgctg ctgtaacaaa
65761 atatctgaga ctaggtaatt tataatgcac agaaatgtat tggctcacag ctttggaggt
65821 tgggaagtcc aatgtcaagg tgctggcatc tggcaaggagc cttcttacta cgtcatcaca
65881 cggcaaaaga caagagaaac aaaaagcgga ccaattcacc cttttataat ggcattaatc
65941 ttacccacaa ggtcagatcg cctctcagag gtcccacctg ttaatactgt tacaatgaca
66001 atttcaacat gagttttaga ggggacaaac tcatgtctgt caaatcatgt gttattcaaa
66061 ccacaagtta atttagtcat tttgaattct agttgacaaa attatgcatc attttgacac
66121 cttgttttta gcaagaagaa tactacaggt tagtatgtag ttcagtgatt taagaagtga
66181 aagtcttaaa atagtttttg ttctcaggag ttgcaggaac acctggatag ttactatttt
66241 ccttatttaa caaatccttc ttgagggccc actagatact atgtgctgtt ttagatactg
66301 gaaagtggtg atatttaggc tgagaccgga agtacaagga ggagttaggc caacagcaag
66361 aaagataaaa taaaggctct gaaatgggaa gcagcctggg gtgttctagg gacagagagg
66421 aagccagcat ggttagatcc tgtgttaatc catttgtgtc cctataaagg aacacctaag
66481 actaggtaag ttataaagaa aagaggttta attggttcca gttctacagg cttcacatga
66541 agcatagtgc tggcatttgc ttctggtgag gcctcaggaa gcttccaatc atggtggaag
66601 gtgaaggggа gccagtacat cacatgacgg gtgcagggag gtgccacact cttttaaaca
66661 acaaatctca cgtgaaacaa ctgagcgaga actcacttat caccaaggag atggtggtaa
66721 gccatttatt tatgaggaat ccagccccag gacccaaaca cctcccacca ggccacacct
66781 ccaatattgg ggatcacatt tcaacataag atgtggaggg gacaaacacc caaaccatgt
66841 cagatcccag tgaacaagag aaagaacgtc atgagacggg gttgaagtgt taggtaaggg
66901 ccaagataca tgctttтaag gagttgaaat tttatttgaa atgcagtagg gagcagatga
66961 aggggaagtg gcaagttctg gttaacaggt agggtcattc cggctactgt ctggctaatg
67021 gattagagga gtaccagggt gaaagtggga aaccagatag gaggccatct gattacatcc
67081 atcoctgctc agatgggggc ggcagcagtg gtgatggaga ggagattgag atgggggtaa
67141 gaggaaaaga gggatcaagc ctgacactaa ggttttggct gtcagaaatg gtaggaaggt
67201 agggtagggc tgtatactga ggtggggaag gagcagagaa aatctccagag
67261 ggagaaaatc aagagttctg ttttggatgt gtgaagtctg aagagcctgt gatacattca
67321 agtggagatg tcggtgggct ctgaatgcaa gagaagtctg agctgacggt acgaaactgg
67381 ggattatcag ctcataggta acattgacaa ccatgtaagt ggaggagacc acctcatggg
67441 agagttgtgg atctccaagg tatactaagt gaaaagcaat ttttagagca attcttatag
67501 tacgatccca ttatttgtgt gttcatgcac atacacacac acatatctgt atataaatgc
67561 atagaaaagg tggcagaata atggtcatca tagaccttag agctgagtaa gaaatgacat
67621 gggaaatggc agcaaaggag gatatttaca tttgctctgt atacagtggg ccaggtgttg
67681 tcatgggtgt ttaatattca cttatttagt actcatagtt agcctttgag ttaagtgttc
67741 agattatctc tgttttatgg gtgaggaagc tgaggcacag agagataagc aatttgccca
67801 aagttgcaga ggtggctggt ggtagaatgg gatataaatc ccaggtagct ttgctttcag
67861 agcctaactt tgcagctgtt gctaggtgtc agaatgtgag tgtgtctgta tgtattgtgca
67921 catgtgtgtg cacatcatca gagcttgaag atcttggaag gaatatggcc tgttttтcct
67981 tgccctcctt ccctaccacc ctcaggcttt tctctggctt ctcttttata tggggtgagg
68041 gtttcatata gctaattata aggttgttca aatagtgcca cctcttaaga ttttttgtgt
68101 aggacaaaat tttggataga cctaagagtg gtttttatta ccctgtaagt aaagcagttc
68161 ttggcacata gtaagcacaa gtaaatgcgt gaatgaattt tgaatgaaca gttagctaat
68221 gacctgggta gggttgcctc ttggaattgg gggcagccac atcttttgt gccctcgcta
68281 ctccccctac ccccttaact tcctttgttc tccttgggtt tgtaaaagtg aaaagaagag
68341 aggagctttt tcataaaatt taatacccaag ggtagctcaa agagcccatc tgaaaggttt
68401 ggcagctggg agagtttgtg tggacagcag cccacttctg tttgattgac tctagggaat
68461 gcaacaggtg aattctgtgt ccgtgaatct ggacctgtag cattgtgatt tcttcgtctt
68521 acaggggctt tagtaatagа ggagatggcg actgcattgt tactgctcgt tcaaaactga
68581 tcaagaggcc gggcgtagtg gctcacgcct gtaatcccag ccctttgggа ggccaaggcg
68641 ggcagatagc ttgaggccag gagtttgaga ccagcctgac caacatggtg aaacttcttc
68701 tctactaaaa atgtaaaaat tagctgggca tggaggctgg tgcctctagt cccagctact
68761 tgggaggccg aggcacagaa acacttgaac ccaggaggca gaggttgcag tgagccaaga
68821 ttgcactact gcactccagc ctgggcgaca gagtgagact gtgtctcaaa aaacaaacaa

```
68881  caacaaaaaa aactgatcat taatatgagt catacttagt aaatgctgaa gtcttcaaac
68941  tttagaggag taatgatatc atccagctaa ttactcttaa taatactgaa aaatcaaact
69001  atacctaga taaaatgtga ttgaggaaaa acaaccttta ttagttcaaa gccaggcgac
69061  ggggatggca gcagaaggtt ctctcagagg gttgctgacc acagttcatt cagctctgaa
69121  aattccctgg cagggacatc tatgaagata agtttttctc tgcaagctta tatacttctg
69181  tactcatttc ttggaccttа atatgtaagg tcttcttatc ttgaagacct tacatattaa
69241  gtggaattga gctgtaaata tcttagactt gcctctctcc cccataaaaa tttgccacta
69301  agcttttcat ctcctacagt ttgggtcccc tgaggtatat gaagcaggcc aactaagatc
69361  tgcatagtga actttagta tgtatctagt ttgacatttt catcaattga aagtaaaaat
69421  tttgttttat tcttggtgta acatttttatt tttgcagaaa tgttctagtg ctaatggtgc
69481  ttgaatgtaa gttttccatc attgggttga aaataggggtt gtctagtcca gcgagctcag
69541  tgcagatcat gatgtgtttg tagaaaaagc cctgtggaag agaaatcctc tttcagtaat
69601  attctaggca gtgccagtgt tgttttgttt ctgttcttga atttacctca agagggcaac
69661  gaacacttta ttttcagata aaaatttata tatgatttgg gtcttcattg caacacatct
69721  catgaatgcc tcttgagaag taatgaaagt acaatctggg agccataaaa ccatcctaa
69781  attacactga attctgccaa cacacacttt aaatgttttg ctcttttctc tcagtctcta
69841  tatttttatg agatcatctg gaaaaaaaaa agacctgatt tgtggcgtgt tgttgctttg
69901  ttaaggtaaa gttttactac aaaccccтca taatagagtt tgtatttgtt ttgagggaaa
69961  ctttgtattt gaggaaataa tagtctagtt tgtgctatag aactagagac agaaagtatt
70021  ttcaagtgtt ggcataattg tgaaataaaa agcagcccag agaagttgtg gttttgacat
70081  aatgtggccc tcggaaatgt ttggatttga ccttgccctt ctctctcatc ctgcccagag
70141  tctatgagtg aaaactggtt ggtttgcaca gcgtagccca ctgctcttag atgtaaggtg
70201  atgaacttca tgtttatttt actttтgttt ttgcttgctg actacataga tgtaaactga
70261  ctttcattag cttagcaggg ttttttaaag attaatttta aattaggtta aaaatgatgt
70321  attgtgacct atgagtcagc aagcagcatt taaggttaat agtctgttca cgttagggtc
70381  aagttttact gctgtgttgg ctcaggtgtc cctgctatgt tttcatatgt tgaacctgat
70441  taaagttttg cttcttaaaa gaataggagt taaggtaaag aaaagcccca gcaagcagag
70501  cctggttatt atttatggca agctagtagc aagcagtgtg ttatatatat tctcgtggat
70561  ggataaattg gaaagttgag tgaacagaga gttcaaggac aaaacaggta tggcttttgt
70621  gaaggctcat taaatcaagc aaagtgctaa tcactcagta ctatcagctg gactgagatt
70681  cttcagtagt ctccagagag caacaattac tggtgactgt catcgtgtaa caatcaggct
70741  ctggagatga aaaagaccgg tagtgggatc tgagtcaccc attcactaga atgcaaatgt
70801  tgccaaataa ctccaacaac cttttaaaat agttttatтc ctttttaatc agctttgccc
70861  agaagcagtt ttacattcaa tctttaatgc tccttggctg ttttcacaag atgcaattta
70921  aagggtagtt acccattaaa aagtgagtga gtcatacttt ctccctgtgg aatttтaaat
70981  tcatttcccg ttcctacctc ttcccccgcc ccgcccccca cgcccccatta atgactttag
71041  atcctccaac tatgttctta cctgtctgag aaaagctgaa gtgctaggta atgctaggta
71101  ccaggcccag aagacaattt cgtagacttg cacagctgca acggaagcaa aaggaaccta
71161  cagagacctg agagtgagtg actgtggccc tgctgccctg ggcgtcattt ctggcaggcc
71221  tcaggacctt ctgcatttct gggctttgac gctgacactg cttatctctc actttttcta
71281  ttgaccattt tactttctct tttggtcacc cagatttcca tacatggtga ccaggatcct
71341  taacattggc cagagaacat aggatacaat cttagtcact ttaagagagt tgatatggtt
71401  tttctttcag cattttattt gaaacaaaaa ttaaacagtt tttagtgagc atccacatac
71461  ccatcaccta gattctacga tacttgcttt atcacatatc tgtcagttcc actatccatt
71521  catcagtgtc tctcgcgtgt gcttgcgctg tcttttttga tgaatttcat agtaagttgt
71581  atgcttcagt acacttctcc cgggatactt catcatgcat atcactgact agtgttcact
71641  gtctgcagtg ttttctcttt gaagtaaatt tacatacagt acaaaacaac ttgtggcgtt
71701  ttatatatat atatatatat atatatatat atatatatat atatatatat atatatatga
71761  acacatatat taagtatacc atttgattat ttttgacaaa tgcatatacc tgtgctacaa
71821  agtcctatta agatacagaa tgtcaccgtc atcccagaaa gttcccacat cccacttgcc
71881  agtaaatcct cccctgcgcc tcccagaggc agccgttctt ctgatttttt tccccatcac
71941  aaattagttt tgtctcttct agaacttcat ataaatggaa ccatatagca tacacttgta
72001  ggcctctctc actgagcata gtattttgag atttatccat gtgttgggtg attcattagt
72061  tgttacctat ttagtgctga gtagtattcc attgtatgca gagatcacag tttgtttacc
72121  atccttctat tgatagacgc ctgagctgtt ttgtttgtgg ccattatgaa taaaacttca
72181  gcgtacgttc ttgtgtaagt cttttгgtgg ctatatgtat ttattttctct tgggggaata
72241  aatagacata gaattgctat gtaagtttag ttttacaaga aaccgccagt cattttccca
72301  aaatggctct actatttgta ctcccaccaa taatgtatga acatttggtt gtaccacatc
72361  ttcaccaaca tatggtgtag tcactctttt taatttagc catttctagtg ggcgtataat
72421  ggtatctcgt ggtttagtt tgcttttgcc tgatgactaa tgatgttgaa cacttttтta
72481  gtatgtgctt atgctatttg agtatatttc ctttgtgaag tatctattaa aatctttтgc
72541  ccatttttga ttaggtggtt gtatatccta gctgccagtc ctttgtcagc tctatatttt
72601  gcaaacatga aaacccagtc tgtagtttgg ctgtttgtta tgttaatgat atcgtttagc
72661  caaagttttt aattttgata aagtagaatt tagcagttgt tttctttcat ggttattgct
```

72721 tttctgtatt gtctctaata aaccattgca cgttcccaag gcacaaagat attctcctgt
72781 gttttcttct aatttacaggt ttgagctttc acttacaggt ttatgttcca tcttgaatta
72841 attcttatgt gtaatatgag gtgggggatca aggttccttt ttcccctat agacagctag
72901 ttgctttaac atcacttctt taaagatttt ccttccctat tcggattata tcacaccttt
72961 gttaaaaatc gaaggactca gtaaatgtgg gctgggctct tttctgtttc atcgatctgt
73021 ttttcaatcc ttatgccagt gctacactgt tttgattact gtggcttttt agtgtatctt
73081 gaagtcaagt aatatgagtc ttctaacttt gtaattgttt ttcaaaattg ctttagaaat
73141 tctaggtcct ttgcatttct atgtaaaatt tagaatcagc tggccaatgc tctattaaaa
73201 agtataatgg atttagaatt gtgttaaaac tatagaacaa atggaaagaa ttgacaattt
73261 attgcttctt gcaattcatg aacatagtct atctccttgt atacttaggt ttttaaattc
73321 tcttagcaat cttcattgtt gagattgtat aagccttttg taaacaaatt ctttcaaaat
73381 atttgtatgt gttttggtgc tacagtaaat gaaatgtaaa tttcatttct aaattttatt
73441 attattatta ttatttttt ttttttgaat cggagtcttg ctctgtcgcc caggctggaa
73501 tgcagtgacg tgatctcagc tcactgcaac ctgtacctcc tgggctcaag acattctcct
73561 gcctcagcct ccgagtagtc tgggattaca ggcatccacc accatgcctg gctaatttct
73621 gtatttttag tagagatggg gtttcaccat gttggccagg ctggtctcaa actccctggcc
73681 tcaggtgatc cgcccacttc ggcctcccaa agtgctggga ttacaggtgt gagccaccac
73741 gcccggccat aaatttcatt ttttcaaatt tttgctgcta atatatatac atacggttga
73801 tttttatata ttaatgttat gtcataagac cttactaaat tcactactta attctaaaag
73861 ctatttttgt aaatcccttta atatttactt cctaaacaat catgtcatct gcaagtacag
73921 tgcatttcac ttttcccttt tggatttgta tgctttttctt tctcttgcct tactgcactg
73981 cctaggacct tttcttacag tgttaaacag aagtggtaag agtgggcgtc tctgtcttgt
74041 tcccagtgat acagggaaaa cattttttatt tcagtattaa gtccagtgtt gcctgtgggt.
74101 tttttatagt tacatgtatt agattgaata agtttattga aagggtttat cattaactca
74161 tttgtctgat gctttctctg catctattta aatggtcata tgatttttcct ccttttatttg
74221 gtaatatgga tcatttttgat ttttttttaa catttaaacct cacatgccta ggatataaccc
74281 tattatatca tcatctttac atattgttgg attcaacttg ctaatacttt gtaagaggatt
74341 tttgtgtctg tgttcataca gggtggtggt ctgtaatttt cttttttata attttgttgt
74401 caggtattcg ttgttggtat tagtgtaacg caggcttcac aaaacaagta aggatgtgtt
74461 gttccctccc ctgtttttctg aaagtgttca tgtaacatga atatgatttc ttccataaac
74521 gtttgctaga actcaccagt gaaactatct agggctggaa ttttctttat gggagggttt
74581 tagatcataa ttcagttcat ttaatagata tagagctatt catattttct gtttcatctg
74641 tgtccatttt aaaaagttac gtttttcaag gaatttgtct gtttcattca ttttgtcaaa
74701 cattttggta ttatgttgcc tttattaggct ttttaacatct gtggaatctt agtgatcacc
74761 cctgtttcaa ccctgatact catcatctgt gttttctctt tttttcttgt ttacccgagt
74821 taggggttta tcaatttttgt tgttctttctc aaagaagtag cttttggttt tattttcctct
74881 actctgtaga cttctgcttt tattttttatt ctacttttct tccgtttaat tgctcttctt
74941 tttctagtga tttaataagg tataaaagct tggccaggcg caatggctca cgcctgtaat
75001 cccagcactt tgggaggtga ggtgggcgga tcacctgagg tcaggagttc gagaccagcc
75061 tggccaacat ggcaaaaccc cgtctctact aaaaatacaa aagttagcca tgtgtggtgg
75121 cacgcacctg taatcccagc tactgggaga gctgaggcag gagaatcgct tgaacctggg
75181 aggcagaggt tgcagtgagc caagatcacg ccactgccct ccaggctgga taacagagtg
75241 agactccttc tcaaaaaaag agaaaaaaag cttggccatc atttagaca ttttcctcaa
75301 agcactgctt tagctgaatc ccacacattt tgatatggtg tattttaatt attattcaat
75361 tcaaaatatt ttttcatacc ctttatatat atgtatttga tccatggaat gtatagaaat
75421 ggggtgttta atttccaaat ttccagacaa tgaggttttt cttgatatct tattaatttc
75481 taatttattt tcatttggc cagagaacct actctgtata atttggtgt tttaaaattt
75541 attgagactt gttttgtggc ccagcatatg tggtctctct tggtgaacat gccatgtgtg
75601 tttgtaaaga atgtgtgttc tcagttgctg ggtgtcatgt tctataaata tcagttaaac
75661 caagatggtt ggtagtagtg ttcaggtaaa ttttgttttt tattctttg tagttctatc
75721 aattgctaag agattgaaat ctccaagtat gattgaggaa ctctgtacat ctctcttcat
75781 ttatattgat ttttactgaa tgtattttgt aaatctgtta ttaggtacat acacatctat
75841 gattgctgtg ttttcctgat gtatgagctt ttcaccattg tgaaattacc tctttatcat
75901 catgagatgt ccttccgcat ccctggtctt gcagtttact tggtgttaat ttagccgtca
75961 tgtgcttact gtttgccctg tgtattatcc ttttccatac atttgctttc cacccatgtt
76021 tctttatctt gaaaatgcat ttctttagac agaagtctac agtaattggc tctttttttt
76081 tttatccatt ttgctcgtgt gtgcctttta attggagtgt ttagtctgtt aacatttgat
76141 gtaattattg atacatcagt ttaagctgat ggtttgattt atatctgcca gttaatcat
76201 ctcctcactt tggttttcag tagccaagaa taalagttgt aatgaatact attatggtct
76261 aattctttat aatgtatttt ttctatatcc tttaatagggg aatatcttct taagagaaag
76321 gtagaggact ccttatatct agtacaatgc ctaagcata gaattctggt acttaataaa
76381 tgctaagtga atgcggtgga aagaactgtc ccttaagaat caggagacat agtctccaga
76441 cttatttata ttattatttt gcattattac ctggttaaac tatattatct ctaaaattat
76501 atttagtttc ctcatctata aaaatgagga ggtttaggac tatattatct ctaaaattat

76561 acctttctgt catctatgat ttgaagcttt ctaatgaaga gaatttttat ctaaaagata
76621 tgttcacaag ttattcttca tttagcaacc actttctgac aatcattttc tataatgttt
76681 ttatgtatat aacccttaaa tttcaatgtg gatataatat taaaagaatg caatatctgt
76741 gattcttttt ttcttttcta ttaataatgt gttgctgctg gttctttagc tacacgaggg
76801 gactacaaaa tgatagtttt tgtcagccat gaaaaaaatc aaacctcaaa caaaatgtta
76861 taagctgttt ttatatatct taagccctgc cagctaatgt gatagggcac aagggtcttt
76921 gattagtctg taagctgcag tgccaccagg ttggtttttc ataggtagta ctcattttta
76981 aatcaaaatt ctgtcgttac ttcattttgt gttgggcgtg gttaatttat agaacctcat
77041 gatataacca ccaatatcga ggaagcagac ttgactacca tctcaaaaaa agattggggg
77101 taatagttat ttttaaatcc tcaagcacat caaacatcca actcagttaa gtctagagca
77161 tcactagcag agcattgggc agaacttcaa attttattga ggtattttca agatagggta
77221 atagttaaga agaggaattt gttcatggtg ctgctgccaa ggagttacac caataactca
77281 aggtgttatc aacaattcaa acaaatctgg ctgttcaaag aagtgagtaa actccactga
77341 cttgttttgg gaccgtagat ggagaagaga ttgtatgttg tgactaacga aaatgaatat
77401 ttcatctctg taccattttt tactgtgcaa tttggtttga acaggttgag tatgaggttg
77461 cagcatgtcc acacagggaa tgttctgtaa gccattcagc aacttgagcc ttgagttctt
77521 gtgagagttt aagcaggact agactcaggc acatccagtt gcagtaagga cagaggtttt
77581 gaaagaggag ctgccacgaa ttatttgtaa tgagaggtgc ccacctcttt gataccacag
77641 cttcttggag tgaaacaaaa gatagtttcc agaagataat aaagagactt taaaatcagt
77701 gtgctatctt ccttccatca gtgtccccct ggttgggccc ttagtgcaag gagacagtaa
77761 taatagatag tgcttctgtc aaaaggtcgc tttcttcttt ccagaaatag aaacatgctt
77821 cccaagaaat aatctaaatc tatttatatt tctgccactt ctagcttttt gttctgtagt
77881 catttctctt tttttttttt tttttttttt tctgtatgtc ttatcccccc agctagattg
77941 ttaagcatgt ctgggacagg aactattata tttttacttt ctgaagaata cctggcctac
78001 tgctaggcac cttctaaggt taactttttg caagaggaaa gataagcggt agatgtatct
78061 ggaggctgct gttggagtga agagagacct cctatgttcc cagttatgcc taattcattt
78121 attccttctt caaatttgta attttttttt aatcaacgga gaatttttag tgttgaagcc
78181 ttttagcctc tagacatgtt tgagcctgct ggctttcagg ggcttcctgt ccagatggag
78241 agacagacat aaccacaaat aacaaggctg actacttgta gtgtgggcag ggtgcttggg
78301 aatgggagca ctgagatctc actgagggtg gaggggttct gggaagatgt cattagggga
78361 gaaatgtatt ggagctctgt tttgaaggct ggtagccttt ggtttttgtt tgcttttaaa
78421 ttcctgggtt attgtcccat ttctcttcac ccctgctcca caatttttaa aaattctgtc
78481 aacgtaaggt tttgacttaa gctatgcttc acagagaaca tagcatcttt tatagctggt
78541 gccactccta tggcatacag aaaagcgtag gattcaacat aaccccacag tgttgagctg
78601 tacaggctta aaatgaacct gtaataccac aaaaagagca gtggaattgg aatcagagga
78661 tccttttgga gtcttggcct tgtctctcga gaagttgaca gagttgctgc atgccgaaga
78721 acttgtagcc cccaaagagg tatgggagtt gaactaggta ctgaaggaga gccatgcttt
78781 tggatggctg tctaagtggc acatactgtt ggatagctac ctaaatgata caggggggatc
78841 atattaatac caggccataa agtgtcagca cagattggtt gaaagcctgt atgcgcatat
78901 ttgcatatta aagaacagtt atgttgatat atttacatct ctgttaaatg aagaatcaga
78961 tttggtgaga tgtaggatta gatatagtat caaaaaattt tcatgagaat acagtaagcc
79021 tatgggaaaa attcattgtt ttgtcattca aatttgatac aaatttctgt ttaattgctt
79081 ttcagatgMa aatacaattc tggaaagagg aaatatagtg aaagcctttt tataaatata
79141 aaatattttt tcaaaacttg agttgttttt ttcttccacc atttctgttg ctgcaaaagg
79201 taatgacatt tcccgcctga ggaaaaacat ttttgaaatg gagttaaatt attatttgag
79261 aataaggttt ccttctgtgg cctgtactat attctgatga cttataaaga gaccttgtgc
79321 agcagtgtcc tctgtatgtc cttggtgggg cctttgacac tctgcaatag gaagactagc
79381 taataaattt tctctttcct ctacacaaat tcccatttgt gcaattgcct cccctctagt
79441 ttttcccagt gatgtaagct actattatgc caccacgctt gctaacttaa tggtatcact
79501 tttaagaaat actgcaggtt ttttaaaaat accagttgga Rtgcctcatt ctaggatatt
79561 ctcatttact tttaaaaacg tcatttagag ctttttgctt tctggggttt tttggtactt
79621 ttttttcaac ctttgtatgg tgtgctttct ccataatata tgaatattta tttttatttg
79681 aaaaatgttt tccctcaaac ccaataattg atgctggagg aaggtgtgtt acgtctctcc
79741 tgtggcatca tgtactgtta ctgcgtgcct tagtacccac ctgtttaagR ggcacaggac
79801 ctgatgattc tattgtttca gagaagccaa attagtttgg atcctgtctt aggcaagatt
79861 tgataagatc tgagcccttt ttctgtctca tagttcatct tttagtgact ttgaactagt
79921 tgtttacctt tagtcctgtt gcctgtggta atcctaccta aaacctcgcg gaatacagaa
79981 ataaacaatg caaaagagtt caaatgtcca gaatgaaaga tttgagaatt tgttctctag
80041 attggtgatt cttagctttc ttaattatta ttggcaataa ataagtccgt tttattgac
80101 aattaagagt gaaagagtga acctcatgga attagttaca aaaattacag aaattttatg
80161 atttttactt ttcagtaaag aacaatgaac ttcttcagaa agaaggaaaa taaatgggaa
80221 atttttttta aaggcttctc tcatcctccc cccaaaattg agaacattgt agaagggtgc
80281 actaagaaga atgatggggt tctaagaatt gagagatgtt ggccgggcgc agtggctcat
80341 gcccgtaatc ccagcacttt gggggccga agcaggtgga tcatttgagg tcaggagttc

```
80401  gagaccagcc tggccaacaa agtgaaaccc cgtctctact aaaaatacaa aaaaattagc
80461  tgggtgtggt ggcacgcacc tgtaatccta gctactcggg aggctgaagc acaagaaatg
80521  cttgaacccg ggaggtagag gttgcagtga gccaagatcg cgccactgta ctacagcctg
80581  ggcaacacag tgaaactccg aatcaaaaaa aaaattgaga gatgttgaaa agcagagaag
80641  tctggggtgg gtccacgctg agttgtctaa gcagtgtggt aactggaata cagagcaagg
80701  actttgaagt caggtggacc caacttcaga tcctgactcc gattttatta gctctgtgcc
80761  cttgaacatg ctgtttactc cctttcagct tcagtttcat cacttgtgaa atggaggtaa
80821  taggacacac ttcatagagc tagtgggagg attcagtact agagtgtgtg gcacagagct
80881  tggcccacaa cagcctctgt aaatgtgagc tcctgtcgcc tcacttcact agccctgcta
80941  gcaagagact tacttctctg cctctttggc cagcattaag gccactaact gagacagcat
81001  gaatctaaag tggtgctcgc tactctgata catgatttta gtaaaagaca aaaatgattg
81061  gtaattttgt aaatcattgc taagattaat agactaggtg aaaaggcttt tgtgtatata
81121  gaagacattt catctaaaat attcctatag tcattacata tgccctcccc ccttttttct
81181  cttcatttta aaatatagag tgggaaataa ataatgtaga tggttttcac ttatgtgaaa
81241  aatggttgct aggaattgaa aaatagggtt tcacagttga aatcactgct ttcaaggaga
81301  ttatggttgc agcttactgc aggagaataa taatgataat gatgataata acattactat
81361  gctagctcag tcacgtcaat cttatgaggt gtagatagtg tattatcctc attttgcagt
81421  taaaggaacc gaagcacaga ggttaatagc atccccatgt gcatagttag gaagtagcag
81481  agccaggatt tgaactcagg cagcctggct ccagagccta cactctttac cactatctca
81541  tactaggagg acagagagaa ggcagttttt tgagacagag taatgtctta aaacctgcaa
81601  caggttaatt attttagatt tgctctacag gtattctgag agagacctca caaagtgtat
81661  tggaattact attgaaacca gaccagatta ctgcatgaag cgacatttaa gtgacatgtt
81721  gacctatggc tgcacaaggc tggagattgg ggtgcagagt gtttatgaag atgtggctag
81781  agacaccaac aggtaagatg gtggcaggtg atcttgcaca agtcttcctc caagttcacc
81841  atttctcta cattcatacc cagccttttc tccttctgac cactcttagg gaaagaagta
81901  tggtattcct tcctttttag agttctttct tctgtctgtg ttcttaattc cattcccctct
81961  ttccctcatt ttcagtcttt ctctagtggg tcttttccag cagcctgtaa acacactcat
82021  ctctctcctt cttcttgtcc taagcagcct tgtccatata gagagcaggg gagaggactc
82081  ggggttagta gtttaaagca ggagagaagg ccaagaacaa agaaaagagt ttgaataaaa
82141  aggacatcag ggtaatgttt aagagattca tttttgtgga gcaaatacca actagcaaaa
82201  agtttggtga tgccatggtt gtaaactttg agaaatttgg gagtgcaaga aaagaaggaa
82261  gtaagagttg ttagagcttt attatgttcc ctctagaagt atatctttta gttgaaaaga
82321  aaatacccgc gaaaggttaa ctgtataaag aacttcacag ttaattgcta aattagtgga
82381  gtagggagaa caattgagag tttattaggc agctgagatg attgaccgag aattctaacg
82441  gtgggctttg gaggaaggat gtgttgagtt ggatgttaaa ggccccttta ttctgtagga
82501  tttgggtagg tgtgattggt gttgtgccag gagaaggaag caaaggggaa ctagggaaac
82561  aagcactgat cagcatctta gaaacaacca agaggaatgc caggccgagg aggatggaat
82621  tttccctaa ggaatagaga tctgttgaat attttttagc atgggagaga atctcatgga
82681  tatcatgttt aattaagaaa gagtaaccga ataggatgct cttatgtggg aaaaggcttc
82741  aaccagggaa actgtggagt gctgtagcct tcaagggctg tgctagagag acagttgtgc
82801  agatggaggg gaaggggagg ctttctgaag aatacgacat ctgagttggg actttcatgga
82861  agagtctgag ttggtcaggt gcagaagagg aagattgagg cagaaagaaa ataatgaact
82921  cctagagatg ggagtgccat agcacatttg aggaatttgg agtggcttag tttgattaga
82981  atgtgaaata ggagagtgat aagaggtgag gctgaaaagc aggcagaggg gctgattatt
83041  aggggcctga ggagtcagcc cagggaggct ggacatgaat ctaatggagc aagccaccag
83101  cacgcataaa gctacaatgt gatggagcat atctgcagct tagaaagatc gcttacagtg
83161  taaggggcag tcagagaaga gcaagttgga agggagatca ggtacgaggc tgttacagaa
83221  attaggcagg aaatactgat gtcctggaaa gaagtgaatg gtggtgattg gtgactgatt
83281  ggaagtgagg ataagagaga atgggaagtc aaggaggctt ggaggagaatg tgggtttcat
83341  ttggctacac taagtttcag atacctgtag aatagccaag tgaaggtttg cttagagca
83401  gggctaggca atagacagtt cagcagtgat caaaatgttc tgtgcctgca actgagtttt
83461  ccattttaat tcttctaaat ataaatttta ataaccacat gtgcctagtg gctgtcattt
83521  taaatagtgc tgctttaaag tattggttat ttggggtttgg aattcatgag agaggcctgg
83581  ccttgtccta ggaattggga agtcatcagc aaaaagacat tagaaattga agccatggaa
83641  atggttggga gcattctgag agagtgagat ggagtctgtg gtttctagga tccttctgcc
83701  gtgaatggga acaccttcgt ggcagaagga tagccacaag acttcagttt agttgcccaa
83761  aactattgtt aggacttgtt tcctgctgga ttggctctag aatgccaagt taagatgatt
83821  tatccacgtg acccccaaatg actctgcctt ctcactaagt cattctctct ttctactgtt
83881  atttaaggat cctccaaacc caccagtgaa atctattttg tatcataggt ttcactcttc
83941  ctcccctgtct acaaatatt tcacaagatc tttaaaggaa agaacatagc agcttgctgc
84001  ttctgcatgg ttttgagctc attttaattt ttaatatagg tatttacatt cataagctta
84061  ttttgactgg tgatgctaaa ccaaatatt ttaatacaca ttaacttttg ccatcccaat
84121  gctttacttt caagacttta agtagatgtg taagagaatt atctcagaaa
84181  taaagttatt tacttccagg cctcctgaga ggtggggatg taaaaaatga ctttctgaga
```

84241 tgtcttttcc cccagccata tgattttggt tatggaactt ctgttacctg tctcagagat
84301 tgttttcccc ttgttccttg tgttaacttt gtcacccatt tatttgtgta acagatgtta
84361 cacaaatagg tagtgatttt cacaaggtagt gatttttctt ccttaggggc cacactgtga
84421 aggcagtgtg tggtcattt cacctggcca aagattccgg ttttaaagtg gtggcccata
84481 tgatgcctga cctgccaaac gtgggactag aaagagacat tgaacagttc acagtaagtg
84541 tgacttcagc caggcgcatt cagaatggct ctgcatgttt cttatcccat ctggtcttgt
84601 tgcttgttca ctgttgatgt tttccagtgt taaagaaatg catccttatt atagaatatt
84661 agaaacacag tagggtaaga gacatcaccc atagccccat cagacaaaac tcttaacatt
84721 ttaatgaatt ctttccaaga tttttctatg cataggtttt ttgggggtg aggttgttta
84781 tgcaaatata acacagacat acaaatatat atgacatagg aaattattgt aatagttttt
84841 tcacttaaca ttttaacaag catttatcca tgttgtagcc tggtctctgt taacatgtta
84901 acatatttaa atgtcttttt aatttaatat gtcatacctt gcttaaccct ttgcaagttt
84961 ttcagaattt aagatatact ggtttttttaa tattatttaa aaaacactgc aggtaaatga
85021 ctttatgtgt ataatttttt ttagtattta ggtttatctg tttatgataa attccatgga
85081 gtagaattat cagggtaagg tagaaacatt ttaagaatct cactgtatta ataagttgct
85141 ttgcagagag ttataaacaat ttatactcat ttcagcagag tttttcttcc caaataattc
85201 tctcctgttt attttctata tatgcttata gatgcatatg cacatatgta catatatttt
85261 actgtttgct agtttgatca ataaaagtgc cattttaact tgcattttga aattgtaata
85321 atacatttct caagtttgta tttactaatt acatttcttt catctttttg gaattgtgtg
85381 tttttatcct ctgactcatt attctattga gataagaata tttttagtat tagtttatat
85441 gaatttttta ggtaaggaga ttatggactc attggttttt atatttgttt taaatatttt
85501 ccttaaccta ttgttgacct tttacttgtg cttccattaa gtcgatcttt tttttccttt
85561 ttttttttt tcttcaaatg cctctaagct tagaactgcc tttctgttct ttgaatttta
85621 actctgggtt gttttattgt tgttatttta actctcacag tttcttgatc catgttaact
85681 ttgttgtggg aaatgagatt ggtcaggcct tttgtttttc ttcagattct ccgatagggc
85741 aagtgtgttt taagatgatg acgatattta tcaagttatt tcatctataa aagtacttta
85801 aatttgtctt gtttagaaaa atgcagttta ccatgtctta tttgtgaagt taataattct
85861 ttcctctcaa gaagtttact tttattattt tttaagctgg tgaactgcac ctgaggacct
85921 gtttatgaga taacattaat tcacagatat ccctcttcgt aattccccca caatggatat
85981 gtaatagact gtgagtctag tatcctcccc tcagtaacta atagccaggt gctcagacac
86041 caggccaaaa aggcacctga aacacacttt ttattatcat gattattatt attattatta
86101 tactttaagt tctagggtat gtgtgcacaa cgtgcaggtt tgttacatag gtatacatgt
86161 gccacgttgg ttggctgcac ccatgaactt gtcatttaca ttaggtattt ctcctaatgc
86221 tgtccctccg cctgcccccc acccacgac aggccccggg gtatgatgtt ccccaccctg
86281 tgtcccagtg tgaaacacac tgttctttag cacagctcct agggagacca gtaggatagc
86341 cagaactcat aaagttaag tgctcctgaa aaatatagta tgtttcatac tgtaggaagc
86401 catagcaaat agctgagtct cagtacatat ttccttggt gtcttcaaca taaggaatag
86461 ttcagtaata acattgcaag gacaaccttt cttgtaaaca gatttatttg ctgtttgtta
86521 gtctttgcag ggaaactcac agggaatatg agtggatcat atttctttc taactgcatc
86581 ctagtaaaga gtaacagaag ggagctaaaa tgaaaaatct gagttctttc tagagaagaa
86641 ttctctacaa attaaattgt tttaaaataa ataagtttta gaaattgata agaggcaaac
86701 agctcagtag gaaaatgggc aaaaaacttg aacaagcatt tcacaaaaga gaatattcaa
86761 atagccaata aacctatcaa aaagttctca aagtaattaa tctttcaaaa agcgaaattt
86821 aaaactacat ttggtctcag ttttctacag caccttggtc ttgtattgtg gatataattt
86881 atctttctt atctctctga agaaatttat tacagatttt ttttatacat ttttattttc
86941 tgtatgcatt gcctctgttt cctccaagtg ccttttgttt tcttttttgt ttggttggcc
87001 ccttaatgta cttggctttc cccaagttta tgatgatctt caaccagttt cttatgcctt
87061 ttttttttt tcctgagagc ggagtctcgc actgtcattc aggctggagt gcaatggcac
87121 gatcttggct cactgcaacc tctgccctcc gggttcaagc aattctcctg cctcagcctt
87181 ctgagtagct gggattacag gtgcccacca ccacacctgg ctaattttgt gtatttttag
87241 tagagacggg gtttcaccat gttgaccagg ctggtctcga acttctgacc tcgtgatccg
87301 cccgcctctg cctcccaaag tgctgggatt acaggcgtga gccactgcgc ctggcctaaa
87361 gcgattcctt atgcttttaa gagtaggggt ttgaaaagcc ggatggcaag gcctgtgtgc
87421 ctagcttgca ggcgtgcttc actgaagaat gttcttttag caataagcgc ttctttcttt
87481 atgggattcc taaatgtcag tatcgtgaac tcttacgtag agccatttga ttcatccaga
87541 gatgaactct ccaacttcct gctttgggct gagtggcctg agtatatctc aggaagttgg
87601 ttgctgacat ccagagagta gggcggagag tccaccagtc tatgtgctgg cttttccctg
87661 ttttcagcct tggtcttcat ctagaccttc ctttgtacct ggaatctcag agcgcagagg
87721 ctttccagtt tctccaggga ctaaatgttc tcatctgcct gttcgggaaa ggctaagggt
87781 taacgggataa ttcctctat gtacacactt gatccagtac ccctgttttt atttccatgt
87841 ctctcctcca tcctgcccag ttcttggtac ctctgatccg tgaggctttc tggaactctg
87901 cagtgtgatt gagcaggcct ttcgttactg tctccttttg ctattttctt tacttgcaaa
87961 gtcattcaca agccttccta gttttctgtct ttgaagaatt tgttgccatc ttgggtctca
88021 ttcttgcctc ctttcttgtt ctctttgttc ttctgggttt atacttttta aaaaattctt

88081 tcctgttcct ttttttttt ttttctttga gatggagtct cgctctgtca cccaggctgg
88141 agtgcagtgg cacgatcttg gctcactgca acctccgcct cctgggttca agcaattctc
88201 gtgcctcagc ctcctcaata gctgggatta cagacgcgca ccaccacgtc caggctaattt
88261 ttgtatttt agtagagatg gggtttcacc atgttagcca ggctggtctt gaactcctga
88321 cctcaggtga tccacctgcc ttggccttcc aacgtgctgg gattacaggt gtgagccact
88381 gcgcctggcc cctgttactt tagtgtggtt ttggagggaa agaaaataaa cacttttttta
88441 aattctctag tgtaactgaa aattgagaac caatcaatttt tcattctttc caaaggaatg
88501 tatcagcctg tatgtctccg aaacttatta tacaagcacc agaaatactt ttctaaatcc
88561 catgttcaaa tgtagattca gactgggtga acaatggctt ccatacgtgc tctttgtggg
88621 atggctgcag aatatttatt aaagacctga tgattcttta aaatataaat gttacaggaa
88681 aatcacacaa ttacagaaga agatctctga aactaaatag tacataaaga atacagcatt
88741 taagaacgtg acagatgtca atgagagatg gaaaagtcta ttgttatatt tctttgtaaa
88801 gcaagttaaa caatgaagag ctttggaaga ctaatgtggc aaagataaaa agtatttttc
88861 cagtttacaa gatagagccc tgccagctga gtagatactc ccaccaaggt gggagtgaga
88921 ggggactgtg agtccacttt catttctcca aaatatatta tgcaaaacaa gattaggcca
88981 aattatcagt gcaaagtcat ggaaaggaga atgcctggtg tctcattgct acatcccaaa
89041 ataaagaaag aaagcagcca gctggggtga tgtagtataa gaaatgactt gccaaaagta
89101 gttgagttag atctattgct cagtgtccag ataacaaatg gacaaggtgt agcccaggat
89161 aggaatggtg ccagttggtt tagggacaga gtagtcatat ccagggatca gcaaactttt
89221 cctctaaagg gccctatagt aaacatttta aattttgtaa gctagatgat ctctgtcaca
89281 acttttgaaa tgtaagcaat taagtatatt ccattattaa agaaaggtat actctagagg
89341 tgaaggcaga cattgaatag attgtcatgt gatgataaga aagaggtaat actggttcta
89401 gtgggatttt ttttaagtgg gacagctagt attgaaagt cagaggggcc tctctgaaga
89461 agtggcattc aaactgaaac ctgaagatta gctagataaa gaaaaattga tgaactttcc
89521 aggcaaagga aattgccttt gcaggagtgg aaaggccaga tggtgagggg tggctatgaga
89581 tgagattgtg caggagacaa gctggaatgg tgaggccta gtgcagtcca gcacacactt
89641 gctttgcccc agtgagacta cagaaacaag gagtttctgt tctgtctgta cgccctacct
89701 ggtcagaagc aaaggctgcc ccagggccta ctgggtgtgc cagagaagct gtcagggtt
89761 gagatttcac cctcggtgat ctctgcataa ctaatggaga agtcattttc tgttctctat
89821 tacaaggagt tttttgagaa ccctgctttt cgtcccgatg ggctgaaact ctatcctacc
89881 ctggtgattc gtgggaccgg gctttatgag ctttggaaat caggaagata taagagttac
89941 tctcctagtg acctggttga attggtggct cggatcctag ccctcgtgcc tccatggact
90001 cgagtgtacc gagtacagag gtagtgtgtt atcttttatt cctaaaatag ttggtgacta
90061 gtctgtttac tatttctcat ggaaatagtc tgatttcata ttgagggttt tggatttttc
90121 ttaatggaaa taagataact ggaatgctat ctgtaaatag ggagggatgg aaatcatagc
90181 atgtctaagc cactttgcca ataacgtatt tatttatcta cccattcatt catgagcctg
90241 gagacagagc catgacggtc aatagtcatg gtgcttgctt ccgagcagct tatggttctag
90301 ttcagtgttt cctcttccag gtctgcttcc atctagatgc agtaatgggt atgagcataa
90361 gaagtgtggc cgtgtgtgca atctctgttc tagagcctct gaaagaaaaa gtagcaacaa
90421 tcactcttta cagatattaa tgtaaatgtg gaggaaaggt gacatatttc tgatggcttg
90481 aagaaaacaa aataatctga actgctttct tcctagaaaa gagaaagtaa gatctcattt
90541 acaatcagga accttatcta cctatttata cttacataca tacatacata tatactggaa
90601 acataacatc acagaaaaat tttagaagcc ataaagttac ccgtatacct acaatcctaa
90661 caaagccaat tcccacacac acatttcccac caccctgcca aaaactacc aggttccaat
90721 attacaaatg caaggccaga aggagactgc aaatgcatta caatcagctg ctagagcagg
90781 actccactga gcacagaaac tgtgtgactg atcatgtaaa gcaatgaaca ctgaaaacaa
90841 gcYgaattaa ctacttaagg agaattatga aggatataaa gtaactgact tgcttgaagg
90901 tcaaaggaca tttacatgat acttctgctg catactgatt tctcagtttt aaaatcattg
90961 gccaaactgc aggatctRaa ttgcctatat ggtctctatt tttaaaaata cacctaagaa
91021 tactaaggag attttaatag aaaaatcaac tSttgaaatt gcttgtgtgg ccctccccct
91081 tgttgttcaa cccttctgaa gcaattcagt ccaaaggaca ttaggtggtg YRgagcagtg
91141 taggtatcca catgcaggag gcagggagcc acagggtcca gagcagggtg agaaggtcac
91201 tcattcacat gcaggaggca gaggcgtggt gcaggctgat gaagtcagaa tgtggcgaaa
91261 agggcattca ttcccaccaa gggcagatct ggtacaggat gtcagagctg tacgtcctct
91321 agggggtggt tggggtgtata tgcagaagag gagacagcaa gaaaagacca gttacttaca
91381 gggagttgat ctaatcagca gatatattaa ggatactggg tgctaggttt ttttgttat
91441 cttagaagtc aattacaaaa gttgaaaaag gagaaaatta gtgtgagcac tgtggtgttt
91501 tggaacagga gatagtggtg tgaactcatg gttccaaca tataggtaca tgtagaaata
91561 agtgtaaatg taatgaataa caacacaggt ggccctcat atcttccgat tctgcattct
91621 acaaattcaa ccaactgcag atggaaaata ttcagaaaaa acagtgggtg gttattgcat
91681 ctgtactgaa catgtataga ttttttttttc ttgtcattac tccctaaaca atacagtata
91741 acaactagtt atagtactta cagtgtatta gatatcaata aataatctag aggccaggcg
91801 tggtggctca cgcctgcaat cccagcattt tgggaggccg aagtgggcgg attacctgag
91861 gtcaggagtt cgagaccagc ctggccaaca tggtgaaacc ctgtctctac taaaaataca

```
91921   aaaaatggcc agacgtggtg gcaggtgcct gtaatcccag ctactcagga ggctgaggca
91981   ggagaatcac ttgaacctgg gaggcggagg ttgcagtgag cagagatcat gccattgcat
92041   tccaacctgg gtgacaaaag tgaaactcca tctcaaaaaa aagtaatcta gaggtgattt
92101   aaagtataca ggaggatgtg cataggttat atgcaaatac tacaccattt tatatgaggg
92161   acttgagcat ccatggattt tggtgtcttt gggagtccta gaaccaatcc cctttggata
92221   ccgagggaca actgtacata ttttgtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt
92281   gtgttttata gcaatcagtg tacttagttt ccagtgagca cagctggttt ctagatcttg
92341   gtctctaaat gctctccatt actaaaagga acctcttgtg ccagaaagta aggaagtatt
92401   caaagaagaa aagggaatct ggcttaaagg gctcccattg gccaaatctg ggacaatttg
92461   agcatcaaaa taaatattga tattaacaga ctaataaccag ctgaataaaa taggaatcca
92521   ctagtttata ccaatattcc taattaataa attgtaagtg tgattcagaa acataatatt
92581   tgcagtcagt cttcatcatt ctcagattcc ttatttgcaa atttcctac tcactaaaat
92641   tcgtttgtga ctcaaatcca atactggcat tttcacagtc attcttgggc atgcttagca
92701   gtgaaaaatt tgagttgccc agcattgtca ccagctgagg tcaaacaggt ggtgctctgc
92761   cttctcattt cagcggctac actgggagcc aatgtcottc ttgcagtctg tttcatgcca
92821   tgtttttcaa agttttgtgc agtttttttga ggattcgcca tttagtatgg cccccaagca
92881   tagtactgaa gtgctggcta ttgctcctga gtgcaggaag gctgtgacgt gccttctgga
92941   gagaatacat gttatgtaag ctttgttcag gcatgagtga tgtgccattg gccatgagtt
93001   cagtgttcat gaatcaacaa tatatatcag ataaggtgtg tttaaacaga aacacacata
93061   aaacaaggtt atgtattaaa cagtcgacaa aaatattgtg accagggcct cacgggaacc
93121   taaccttgta ttttccctaa gagcaattac tcagtataca gtgtaagtgt gttggtgaca
93181   ctcggtgtag aatgttaact acttattgcc tgctaacaga actagaacca actaccgact
93241   gtacatagtt gcagagtatc tcccccacca tacttagcaa ttgcagagtg aaagagaata
93301   acctaatagt gggaaaacct ggcagctgat caaagtgaac attatcagta ataggacaaa
93361   tcacaattct aggctgcctg atagaggtta tgagaacgta gcatcactcc tctgttactc
93421   agccagaact tcacgatctg aatccaatag tcaggagacg ttagacaaaa caaaattgag
93481   aaacattcta aaacataact ggcccgtaat cttcaaaagt atcaggatga agaaaagagt
93541   tctaacttga aggagactac acagacatga caattaaata caatgttctg aactgggtcc
93601   tttggctgta aaggacttta atgggacact ggtgaaactc aaatggggtc taggattaga
93661   cactagtgaa gcatccatgt taacttcctc attttgatgg ttcttttgtg gttatgtaag
93721   agaatatcct cgtaggaaat atttaaagta ttctcagggc gttgggacat cttatttgca
93781   aattaacttt caaatagttc aggaaaataa ttatttgtac tgcacttggg actttttatg
93841   taactttgtg attgtttcaa aatctaaact aatacactag acaacaaagc tgcagtaaat
93901   agcattcaca gagacaaaag aaaaagacga tttgcatgta taactgactc aagcaaccag
93961   aaagcagtaa agatgcagct tctcagccgc agagcatggc aacagatagc acaaaatagt
94021   tagcaatttc acatccagaa atacccgaaag taacaaggca tggatcccac aggcaatcag
94081   atgaagaatt tgcatttctt ccctctgttt tcggcttaaa tttctttctg ctgtaaccag
94141   tgagtcaaaa gcagcagaga cattgctata ctattaaatg cttaatttta tagactttta
94201   aataccacta tgcgacatta tcctggccta ccaacaactg agaaaataag gacttgaaga
94261   aaacaagggc agcagaaata gtctctatag gaaaaatgta aaggagtgat gacaggaaga
94321   gtggagaaca cttatatgat acaaccgaaa ggtcatatga taagaaaggc atgacattat
94381   taataagcaa catatgaggc ctgttaagga aacctggctg ttctcagttc ttctgataYg
94441   accccgttac acttatccta tggagaattg gcccatagga gagtcccaca gctctaattt
94501   caggaggccc aactgtcaca tatgtttctc tatcaatatca tcacttatgg agcttgtgag
94561   tgaggagtgg tacaggtgga tgtaggctta agatttcgaa gtgacactct tacttcacac
94621   Wtaggtgggt ggattaaaat gtaatggaat actgtaaaac aagaggcagt ggtgcaatct
94681   ctttcaaaat gtggaattag taatgtcctc gatgagtctg aggacagttt atttttgaa
94741   gatagtgatg actcagttcc taacacagta aggccattgg tgaagagagt catccagagt
94801   ctagctgtga tgtcaggttt ttatgcttta ggattgataa tgtagttaac
```

CHDC1 genomic sequence (SEQ ID NO: 3)

```
>13:44917401-45013900

1       tcaaatcttc tcaaattttc cccatcttaa aaactaaacc agttttctct gctttatttg
61      ttttttagtc aactattaat ctttttcttt cttctagccc ccaaacgctt ggagtaagta
121     acttacacct actctttcta ctttctttgc cttctcctta cctctgcagt ttggatgttg
181     ataaactgtc ctagaactac tctctcaaag acagaggatt ttctgtgtcc cccaagtctt
241     tgYctcttgc atttgctatt attgcaggac aaggacagag ctctctctgt tgcaactcca
301     gtaccaaaca ttacctgtgá gttagaagcg gttcagcaaa tctttgttga atacagactc
361     tgtggtcttt tcctttcaaa aacttcttgt ccatccatcc ttatgcatgc cctgtgctcc
421     atcctagtcc aagcaccctt tgtcacacct cctataccty gtaacactat tctggcttgc
```

481 ttcttcaatt ccaattcatc ctgcagagta tcatttcatt tacatcttcc ttgggactca
541 cccatgactt caatgactat tgctgcaaac tcaatcttct gaattggtat ttttaaaatg
601 taattaatta actgatttat tattatattg attaattata gatgcacaag gtaaaactga
661 acaaacagat atctagagaa agagaagtct ttctctcatc ccattctacc agttttcttt
721 cccataagcc atcactgata gcagtttctt gtccctcctt gcagagactt tctgtgctag
781 acaattgctt cctgattgga ctatggctca ccatcatgcc tggggccctg tcttgaatcc
841 tagccagttg ggctagggtc ttgtttacct cctgggcatt ctcccattgt gggctgtgcc
901 atacatcccc ccaggcaatg atttatgatt tgcttcaatt ggcatagtct aagatgatcc
961 ttgctcttag aagagtatct gggactccag cggctgtgac cagacatgca ggtaacactc
1021 ccctgtgggt attatgaggt attccaacac tgttcaccct cactggggtg gacttccttt
1081 ctggtcagtc ctctatccca accacgctaa ttctggcttt actctctctg cagcaaccag
1141 aaatcgaaga aagtcctaac tggttttact tttgaactgt ggtgagttgt gctacgtgtt
1201 gacctgattt gccaacagat aaaatgagat gaccatgttc ctttgcttct gcactattgc
1261 ttcactgtct agcaggacct ctctttagat gtcgcactgg caggatttga gaaataactt
1321 ggggcgttag acagctaatg tttaaaccct gtgtatgtga atagtgatag catctgggta
1381 tgggaagctt aacgccattg tagccagagg gcattttctg ctaaatctgg agagaacaac
1441 cactctggga gcctctgact agaccctaat gacagcctta agttcggaaa atatccctgt
1501 aatgatatca agagtcttaa aaacggcctc tggggaacat gaaaattact gctttagttt
1561 gatgcaaagt accttaacta caaataggaa gactttttttg tccttttaaa gtccacctaa
1621 tgaacaacag gcctgaaaag gtacttaaaa tattgatttg gaggtacatt ttgatcagtt
1681 gaactgcgat ataattggcg atcgaaagat gacacatcca tgagagagac taccccagtc
1741 cagggtttct caaagtgtga gccatggata acagtcttgc aagatgagat ttattggtca
1801 aatatatagg aaaaaactgc agtgaatcat ctttccttct tccatgttca caatgtacat
1861 tagcatatca aggattcaga gaagtgtgtt agtaaaacaa cttctaaact tttaaattaa
1921 ccctttgtct cccaaactta tttggcgaaa aaatgtttta tgcatagtgc ctgttagcag
1981 cctaaagaac taaggttcag agacacacac actggataat gctgcttcag tttattcatg
2041 caagttaaat gatttacggt catgcgatgc acaatgacgt tttggtcagt gacagactgt
2101 atggaatgat cgtcccataa gattataata ccaaattttt actgtacttt ttctatattt
2161 agatatgttt agatacccaa atgcatactt accacggtgt tacaattgcc tatagtattc
2221 agtattgtaa catgctgtac aggctagctg caataggcta taccatatat agcccaggtg
2281 cataatagga tataccatct aggtttgtgt aagtatactc catgatgttc acacaacaag
2341 aaagtcatct gaaatgtact tgtcagaata tatccccatt gttaagagag acatgactat
2401 attaataaac aaataactgg ttcctctaaa taattcacat attcatcata ttacaaacca
2461 ataatacaat atgcctatgt tataaaccaa taacataata taatgaactg gtgaaacatt
2521 taggtgaacc agttgcaata aagctgtttt ttaatattat ctgttatcta acatttacat
2581 ttgctttttt tttaaagtca ggtatttaaa aatcgatttt cctttttttt tgagatggag
2641 tcttgctttg tcaccaggct ggagtgcagt ggcacgatct cggctcactg caatttccgc
2701 ctcccgggtt caagcgattc ccctgcctca gcctcccgag tagctgggac tacaggcaca
2761 tgccaccatg cctggctaat tttttttatt ttagtagaga cggggtttca ccatgttggc
2821 caggatggtc tcgatctcct gaccttgtga atccgcctgc cttggcctcc caaagtgctg
2881 ggattacagg tgtgagccac cgcacccgcc ctaaaaatct atttctttat aagttaaagt
2941 cttattagtt gatgcctttt ggtccttatt ttctagtgaa ttcacctgga agcctcctaa
3001 acctctggca ggaaccagag ggtttgctac tgctcactga tgtttttttcc ttacaactta
3061 cttaaggaga tctcaacctc cttaagccaa aatattcttt tattattatt atttttattt
3121 caataggttt ttggggaaca ggtggtgttt ggttacctga ataagttctt tagtggtggt
3181 ctctgagatt ctggtgcacc catcacctga gcagagcaca ctggacctaa tgtgcagtcc
3241 tttctctctc accacttccc actctttccc ccaagccccc aaagtccatg tatcattcta
3301 tttttttcttt ttttagacag agtctcactc cgtcgcccag gctggagtgc agtggtgcaa
3361 tctcagctca ctgcaacctc cgtttcccag ttcaagtgat tctcatgcct cagcctcccc
3421 agaagctggg actccaggcg cacgccatca cacccagcta atttttgtat ttttagtaga
3481 gatggggtct caccatgttg gccagactgg tctcaaactc ctgacctcaa gtgatccgcc
3541 cacttcggcc tcccaatgtg ctgggattat gggcgtgaac caccatgacc agctgttgta
3601 tcattcttat ccttttgcat cctcatagct tagctcccac ttataagtga gaacatatga
3661 ttggttttcc atttttgagt taccaaaata ttcttttcat tacaatcagc ttctaatcca
3721 cagtggtcca aaccaagttt tcctcaggtt ttttcaaaat cctattatca ctcataagtt
3781 ctaggtcaga atgttgtctc tccgttatac aattggttat attatctcat ataatttctt
3841 aaaaagcatt gatttaaaaa caaaaatcac acataaatga aaattgacat ttcataagac
3901 catgtacaca tatttatgaa gacagaacaa ggactaaagt ataggttatt gatttatcaa
3961 gactgctcct ctattgtcat tcagagaatg gtcaagaagc cagcttctct gagaatccta
4021 tcttgaggca tagattctgc agtttcttta ttccgcagga actgctgtag aaaggagtac
4081 ttaaataaag tctccctggt ctaggagcca gaactccacc ttaatctggg agaaaacagg
4141 gaaataaagt ggccagaggc tagtagctac tgctttgttg cttcaagaga aggaagtatg
4201 agcctctatg aaggggttga ggtttttttgc tggggacttt ggggcacaga atgtaaaaaa
4261 aaaactgcgt ctggacaata gtcagctatg aagtatttaa aaatgtaaag gggctgggtg

```
4321  cagtggcttg tgcctgtaat cccagcactt tgggaggccg aggctggtgg attacctgag
4381  gtcaggagtt taagaccagc ctgatcaata tggtgaaacc ccgtctctac taaaatacaa
4441  aatttagccc agcatggtgg tgtgcaactg tagtcccagc taattgggag gctgagacag
4501  gagaattgct tgaacctgag aggcggaggt tgcagtgagc cgaggattgaa ccactgcact
4561  ccagccaggg cgacagagcg agacactgtc ccataaataa ataaataaat aaaagggcca
4621  ggcacagtgg ctcatacctg taatcccagc actttgggga ggccaaggtg agtggatcac
4681  ctgaggtcag gagtttgaaa ccagcctggc taatgtgttg aacctgcatc tctactaaaa
4741  atacaaaaaa aaaaaaaaaa aaaaaaaaat tagccaggca tggtggcagg tgcctgtagt
4801  cctaactact cgggaggctg aggcaggaga atccctgaa catgggaggt ggaggttaca
4861  gtgagactcc atctcaaaaa aaaaaaaaaa aaaaaaaag aaaagaagat tagttgatgt
4921  gagcacagct taagaaaatg cttgaaagca ggtgactaga cttatgtatg actaacttcc
4981  ttttaagaaa accaagggtc tcagcaagta cagtagttcc cagagttttt gatttcagag
5041  ataaacaaca tcaaaataat tggtaactga ctttagtaac ctccttttgt tatttttttga
5101  aaaaggatac ttaaaaaaca ctacaattta tgttaccaat tgttttggtt ttttttttc
5161  atcagaaaaa aaaatagtga aggcacagcc tcacaattat atataattt tgaaattaaa
5221  tacattcagg ttcatgaaaa actcaggaca ttgtcctatt ttttttccct catttatca
5281  gggtcatttt ttcatcaact agctgattca catagaaaaa tcctgaaaca catattattt
5341  atcttcagag aaattcatgt tgatgttact agttgcatca aatatctcag ccagacaaca
5401  ttatttgttg aatcttccag gcagcggatt tttttaaaag ggcctgattc ctgcccttaa
5461  tagcaaaagg gtgctgtttt cagaataagt aaacagggta ttaaacaaaa gagagatgtc
5521  catcttcttg aagaaatagt gaagaagcaa gacagcaagg ggaaatggct tgtcgagttt
5581  ctttaatatt tagaaataat caagatcatt ttcaagggtc aagtactctc tcccatttta
5641  agaaaaactc cttcattcag ggaaatcatt tgaaacttta aagatgtatc aacaagtacc
5701  ccataaattt atacaaataa aaaaggacat atcaacaggt ggcaaacctg ttaaacacat
5761  ggtctattat gcaatactta attgattact aatattaatt gtgcactcat tatatacaaa
5821  gtactcccct cgatttgtgag gcatggggag agagttgcaa agatgaatag gtcccttatt
5881  catggaattt acagtttagt aatctgtaga tgggtaaaca aaccacaatg agtaggtcaa
5941  tctaacagag ggactgatca tttgttaaaa agcaaatcgt gggctcatat gcaatccatt
6001  attttcttta aagaagaatt agtggtcttt taaaaaaata tgtatgcttc ctatgatgca
6061  tcacaacgac tcttagtctg aactaaattt gcagtcagcc agaagatgtc ccaaatcatg
6121  tcctgactgc tgatcacaca gactaccacc tggtttcagc tgaagattct tttaattgga
6181  ttttttctg tgtttctgtt tttcactgga ttttgttttt ctctgttcct ctccctgqag
6241  gaaagtggaa atttggttac ttttttgtga tggaagtata ctttcattta ttattattgt
6301  cgttattatt atgaattttg aagccggact tttaaaagcc tggaaggctg cggcgaatgg
6361  catgtgagag gggaggtttg cgggaggata ccagcaggtg gcgcgtgtct cctccgggca
6421  gattagaatg ctttgctcag ggccaagaat cccgcaggaa ttaagggcaa ctatctgtgc
6481  agtcaattca agtgacacag atcatgccat acttaagtgc cgagtccatg aagtcaccag
6541  ttccagcctg ttgtctaggc catcaaactt atgtattacc acttaaaaaa ccagctcccc
6601  tactccaagg gttgcattac tttcgtgctt gacaccccga caaccccgca cccaccccc
6661  gactcatttt ccccaagcca agtcgctcat aggggacaat caagccttaa gaatagagca
6721  aaaataaagg ccctggaaag ttggacatga agctttaact tcaggaaagg aatggtattc
6781  tattaatcgt ccagctggtc tgcccttagg gtgtcagatg ttctctgtcg cccctggtgt
6841  gccagcattg gcctgggtgc cactgggtgg ctgatggcag aatgtgaatt cacttgcaag
6901  cggacatgtt cgtttccatg ccccaaagcg ggaagaagaa gggcacaagg agacttcgat
6961  ggttctttca gctcagactc gagctgtgac tgatttgctg ttttgggtca ctggctttct
7021  agcctctcct ggcaccaccc aatttcgggg agcagccagc tcatctttct cctacgacaa
7081  tgtcttctgt ccccctaaa cactgccctc attttgagtt tttctttcct atgtctgtag
7141  cttctctctg ccgctcagca acactctgt ccgactcgtt ttcgtccctt ggcgctggcg
7201  tctggcccag gggtacactg tgaaggaggg caaccctaga ttctgagggc cctagctcga
7261  atctagcgcc cctctaactg cagggggtgac cttagataca tttattaact tcctctgtag
7321  actcagggga acaacttttg cactcctggg gtccctggat taatgaggta acttacgtag
7381  actccctaaa caagcgtctg gttcattgta agcgcccaaa tgccaggggg catctgcagg
7441  gatgacccca tagtgaatga aaactgcctc ttgggggatct ctgggttaaa cggccagaat
7501  aaatcgcaga attgagagaa ccctctcctg ccccaaacct cactgtactg taaatcccat
7561  tcattgcctc ccgccgtttt atccgtgttc tcagaccacc cccctatccc cgcaacctcc
7621  agtcccctaa agcctcctgg gcggcaaaag gacgcccaga gagaggttcg gcgccctcaqt
7681  tgccccggag cagacgtcca gccccgccgt gtaccgcatt gcgggggcga tcgcggcaag
7741  gcggcggcgg ccggcagaat aggcgcggag gaaggctcag gcgggcaga ctgcgtgggg
7801  gaaggaggag gagagagcag acggcggagg agggcagagc agccgggggg agggcgcagg
7861  ggcgggagga gacacatgcg cgctgccgcc gccgccgcagt ccttagcttc
7921  ccggggacag gaaaccttca agaccgagct gccacggccg cctccccgcc cgccccccat
7981  tctacgcgcc tgcccacacc ctcctcccct ccttccagcg cctttcggtg gagcactgcg
8041  gcactcagcc cgagctgccg ttttccctc gcgggaacg ctgtgcccc cccgcaggag
8101  cggcgggcg gggtgggggg gcccgggaga agatggcgac gccgggaagc gaaccccaac
```

8161 ctttcgtccc ggcccttccg gtagctactc tgcacccact tcatcatccc caccaccacc
8221 accaccacca tcagcaccac ggaggaaccg gcgcccccgg cggggcgggt ggtggcggcg
8281 gtggcagccg gggcttcaac ctgcccttga accgggggtct ggagcgccgcg cttggaggag
8341 cggccaactc cgggggggtg aacctgagcg ccaggaaatt gaaggaattt ccccgtaccg
8401 cagccccccg gcacgacctc tcggacacgg tgcaggcagg tgagtgaggg ccgaggggcg
8461 ggcaggggtg tgggtgctgt ctgggtgtct gtcgtgcgtt ccctaacgcg gtggacagtc
8521 ggagatcttg tcttgctggg ggagggaggg tccatcggcc cgttgtctcc cgaagaaggg
8581 actcgcgtgg gcgcggaaga agcgggccct ggagagggca cggggccttc gcctggtccg
8641 gcgatgcagt gccaggaggg cagggggtgcg ccgggcctct gcgcctgaga gcgaggggtc
8701 tccggctctc caccctgtgg ctgccgcgcc agggaagtaa ccgcggggct gggacttgca
8761 ggcgcgccgc gtgcgcgcag tgtaagtggg aggtttcagg cggctgtgtc ggcttcctgg
8821 gcccgcgca gggctgggaa ctccagcgcg gacagcggcg tcggcgcctc caaccagttc
8881 aagccgtctt tgcatcgagg cgtagcccat cctggtgggg aaaccccagac aaaggtggca
8941 cgcctccggc cgagccaggg gcatcggcgc agtgccgcga gccccctcgg cgacatcgcc
9001 gagcgatcgg gcaactcggt gccgcctgtg aggtgcccaa gtttcctctc cctggcgttg
9061 tgcgggaaaa gagccgccgg gcttgtagtg aatcccagtc ggctgccgct tcggaagcga
9121 tcggccctct tccttccgtg ccttttgctc accgcccaca cagtttgggt cctaccaccg
9181 aggctacctg gttctcagtt acccaaccgt tgcgggggcc ccaggaaagg acggcgtggc
9241 atattaaagg caaagtaatt aacgtgagcc tgttttcctg tgtgagccca gcaagttgta
9301 actcgcgcca ataagcagca taacttttttc aagttacgtc atgtgttaca tacttctaaa
9361 acgtctgctt tctctttggt agttggagtt ccaggagcgg gatctataaa caggaaggag
9421 ggtggtggaa taggattggg gccttagggt ctatacagaa ctgacttggt ttccggccat
9481 ccggttccgc tccctggggg agggttgtg tatagcaag cgcccaacat ttcccagggc
9541 agtgggtgct ccgttttgga gccgctgccc agacctcttg gctgtcatcg cctcatggcc
9601 cagggtcaga ccccctgggt cttggatggg ttgacttcta tcacaggagc acccagttta
9661 atcttgtagt gggcaaggga gcaggcagtg ggttttgga ggctaggttt ccaagtcctt
9721 ttccccctt tcattcaata aacatttatc tagagccta atgaatattt agatacagtt
9781 ctgagttcac tggaggcaaa gatggctctc cagggtcatt aaacttttgta attttggattt
9841 agggatagtc aggaatcggc aaaaaagagg gaatttccaa agttgagctg tcaacagctg
9901 gggagtgtct ttcaataaga cctcttagtt acatcttctc aagtggaact tattccaaga
9961 attgcctgaa tcactgactt aaaaaactac attaaatttt acttcccttc tgctatagag
10021 tgtaccgtga gctagctatg ctatggttgg ctatatctgc agaaaatagg gctggcatga
10081 ctaataataa taggtttgtg tagttcagta aggggcttc atagttgttc tacttcagtt
10141 atgctaagga ttatttacaa agttaggtga acttgatgtg tctgctgtgt tggcatttct
10201 ttgagaaRac cagtgctttt agggatcaca tcttttagct aagacctcgc catgtgaagt
10261 ggatgctgaa agtgttcttg ttggctgtt tatggcaagc ttaagttgtg agttttgcag
10321 gttttatatt atgagctcac ttgcacatgt ttatgctcca ggaaaatcta actggttaaa
10381 attcagaggc tttatgttaa ttcctcatcc aaaaatacag tattatttgg gggaagagga
10441 gtggagggat attcatgttt gtagaaactt aagtcaaccc catcagaaaa gtattcattg
10501 cagctagtta tttacatga aattagaata cccaaatgta ttaaatattt gcttctgcaa
10561 aacgtctttg cctcaggtca aaagctaggt gtaaaccaca tgtactcttt gttctaaaga
10621 taaatttaat tgagcacagt ttcttatttg agagaccaga aagcaaaata aagagttaaa
10681 gttacctccg gtgtacacag tgttgacaca gcgtacatgt aagagttcta gtacagttga
10741 aagtttgagt agtaacattt ataataaaga tagtggtttc tccttgactc atatttactt
10801 taagaatgtc tcttaaaatt agaatggcat atgaagatcc ttaaaggcct aagaggcaaa
10861 gtggattttt ttttccatat attttctaag acagggagtg gtagagcaag ctttttctca
10921 cagttttgtt gtatattaca ggccatttgg ttttacgcctt gtaaaaagtc aggcttctgg
10981 cagccacctg tgcagaactg cacctgggca atatagccca tctgaacaga gtggaaaacc
11041 aagatgtaaa caaagaaaca tagaatagat gtctaagctg tcactcaagt gcatatactt
11101 tattgatagg aaaaaattca agctctcatt ttgagcctat taatttactt ctatttgaat
11161 caaaatagt tttgttgtca gagtctagtc ttttaatagg tgaaacgggg aaagaaagac
11221 tgatccacgc aggtgcagtg agtgacacag gtgtcactga tggaaaggga caaaacagaa
11281 gagccactat cagcactggg tgcgccttctc tatgcgttat ctgcatgatc ttagtcccca
11341 ctaggagccc agtcatacc tcatttatac atgggaagac tgagacagag acaagttaca
11401 taatatgctg aagattatac ctctactgag atggtcaacc ggtgattgga accctggcag
11461 cctcacgtta attcatgttc ttgaccatat tctcatcaag cagaggtaag gggttgagag
11521 atagaatctg ggaggcttcc tggaaattca ttcaaccagc attgattcca caagaatgta
11581 ctgagcccct ctgagtgctg gccactgatc taggcactgg ggcacacaca gtgaccaaaa
11641 gagaatccct gtatccctte ttgtggagtt cattctagtt ggagaataga gagatacatg
11701 aataaattga ttttgcagga taaatagtgt gagttacagg atagatggaa tatcttttgt
11761 ttataaatac acagattgct ttgtattgac tcaggtggtc ttgtagcaag agtataaatg
11821 atgactagta atacatataa tctgaagcat aaaattgggc caaagaaaaa caagtacaca
11881 aatttgcata tgagtaaagc aaatttttttt ttttttttggt gctgatttat taagtagtgt
11941 cgttttgaat gaagaagttc aaaagggtat tttgtacaat taaaagtgaa ttgaaaagga

12001 gtaagaaaag aaagtggctg attgcaggag gttctagaaa ataaaaaaga agcccttaga
12061 cttggcatgc aggacacttg ttgaaagtct tgttaaggaa agtggggaat atttcattgc
12121 taattatctt tttgagttgg ctctaagcag gaaagactat gggccaggca ctgtggctca
12181 cacctgtaat cccagcactt tgggaggcct aggtggaagg accacttgac cccaggagtt
12241 tgagaacggt ctgggcaata tagtgagacc ccatctctac gaaaaataaa atattaggcc
12301 aggcacgata gctcactcct gtaacgcctg cactttggga ggccaaggtg ggtggatcac
12361 ctgaggtcag gagtttgaga ccagcctgac caacatggta aaacctcatc tctactgaaa
12421 atacaaacat tagccgggca tggtggcatg tgcctgtaat ctcagctact caggaggctg
12481 aggtgggaga atcacttgaa cccaggaggc ggaggttgca gtgagctgag gttgcagtga
12541 gctgaggtcg caccactgca tgccagcctg ggcgacagag agagactcca tctcaaaaaa
12601 tgaatgaata aataagtaaa taaaataaaa aattaggcgg gtgtggtggc gcatgcctgt
12661 agttccagct atgcggacgg ctgaggtggg aagcccatag gttgaggctg cagtgaaagc
12721 catgatcgcg ccactgcact ccagcctacg tgacagagtg agaccctgcc ttaaacaaac
12781 aaacaaacaa acaaacaaaa caaagactat gtgggaaaca aagagcttac tcagggaaga
12841 atattgaagt gcagcattaa aaatacccat ttatgtgtga gggaagagtt ctgtaggaga
12901 tgcaaagtat aagacaatac aggaatacat gagatgctaa ataacagttc caggaagcca
12961 ctgaggccca aggcaggtca aggtgaggtg ccaagtagca ctgatggaca ttgtgtgtag
13021 aattcagagg aaaaggtcat tttcatgagg atgcttagga aagactttga tagcagaggt
13081 aggatttgga tcaggttttg taggatggat aggatttaga tagaagtgcc tatgaatatt
13141 ctgtgattgg aaggatggtg ccaagacgtg gagtaagaac ctgacagttg gccgggtgtg
13201 gtgactcaca cctgtaatcc cagcattttg ggaggctgag gcgggtggat cacttgaggc
13261 caggagttca agaccagcct ggccaagacg gtgaaaccct gtgtctacaa aaaaaaaaaa
13321 aaaaaaaaaa aaaagctggg ttcctgtaat cccagttact cgggaggctg aggcatgaga
13381 attgcttgaa cctgggaggt gaaggttgta gtgagccgag gttgcgccac tgcactccag
13441 cctgggcgac agaacaagac tctgtctcaa acaaacaaac aaacaaatga acctgacagt
13501 ctaagattct gtgaataaaa gaaacagaga gggcatttaa gcctgtcttt ctggtcatat
13561 tcttctaccc aactcctgcc ttataatgga gtaaaggcta cagggctctt atgacccttt
13621 aattgaggac tccggaaatg gctgaagcct aggatttgtc agcctgtggg aataacaccc
13681 tagctctgtg tgatctggct ctctcaaatg tctgtacaga ttcaaaggat cttctctgag
13741 atttgtgggt ggttttatct cttgaaggct gacttccaca ccctattccc atcctaaagc
13801 aatggagtcc ttgggatgtt agcactcttt agtcgttgga attcacagaa gacttgataa
13861 caaaatctag tcattttcaa caacttaact ttatttcata atttttgcca tcaatatgtt
13921 tcactataaa tataataaaa tttttgaaat cacatgtgtt tccttaaaat gtatgttctt
13981 ttatagttat atccagtttt gaattatcgt tctgctattg aattaaattt ggtagttttt
14041 aacatacctg ttgctttttg tggtggttac tatcagataa atgcctttgt ttattacatg
14101 tattctaaat attcttccat tcataaacta tgattcatat ccttttcttt cctattacta
14161 ttgtttttttc ttccctgtta aggtatagat aaattccaac atcaaacaaa agcttttgga
14221 acaactcaga caatatctgt agtggttctg aatcacgtct agatgggccc ttccacatgt
14281 ctgtggtata tggcaaaaac agtctccaca aacctacatg ctattctcat tgcttgcatt
14341 acaggctgct ttcttgaaaa ggcaaggaca tactaatcat gcttctagaa taatagcata
14401 caattatagg ccagggaacc tctgggaatt tttggtctgt gccagtttat aaaggaacag
14461 cccaaggttt gaccttcatc actgagatga ctctactgga gagtttgtca gtcactgcaa
14521 catctgattt gatttttggt aggtgtttga tactaggcca caaattagca caccctgtca
14581 tttaaaaatt cttgtttaaa ttattgactg agactttttt ttgtgtgcgt gtgttactgt
14641 aatgaactga aatttcccat ggcatggcat aataactctt tgtaataaac atttaaaggg
14701 tagatacctt ttgaaatcca tgttgacgtc gattaattca gaagtcaaac ttgttttgcc
14761 cgtgctgtcc atctggtata tgtacataga ctttttctat tatatcattc aacttcatca
14821 ttgcttgttt aaacacaagc tatttcctc ttttgtgtat acatttctgt tcccccatat
14881 atatagactt tttatatttc agctgggcag catttacttg ctcttaatgt ctccccataa
14941 tttcccttca ggtgtggtac tgcatgtgct ttttcaaagc cttgataatt taaatggcag
15001 aaatgctatt attaactcca tataaggtgg ttatgggttt gtcactcaRg ccatgtgtaa
15061 cttgaatttt tgtctaagcc tcagaaaaac ctgtttgtga ggccactttt Yagaatttct
15121 tgggcttttt ggaaaattga acgtctgtct tggatattgg cttgagctta gatatggcaa
15181 ttccaccagt gattatttca gtgattgtgt gaattgttag aattaagata atttggtgtt
15241 aattgcagtg attatttcaa gttataagat tRtaatctat tataaaYgtg ttaaggatgg
15301 aaggcacaaa acccaactat ttttcYRtag tgaataatct tttttaatgc ccaactcata
15361 ggaagcctag cttctgttat tgctactagt cttttgttgc atgaaagatt tttgtttttg
15421 catcagaatt ttgccatgat atttcagaga gtaagaaaag aaaaaaagaa aagaaaggtc
15481 agggttccaa gtcagactta atgtaggaaa actaggcatt ctaatataga ctcaaacatg
15541 aaatatgcct gtgttattct tcatcctaat ttaagagttt agtgatattg cttccatatt
15601 ctgcagtaag aaatagtaca tttggaaacc atctcctccc ataaagtaat tcaaaaataa
15661 agtgagattg tttacatgaa tagaaagttg atgaactgtg agaattgggg cttcccttgc
15721 ttactccagc catgcaatag aagggaaatg cttttatagt cagatttctg ttcactgttt
15781 ttcctaacca tatcctcctt cactggccat aaaggaggat atagctggag aaaaaaatca

```
15841  gagaagaaca gtatgtttga tttgcataac agaaatactt catattttgc ttggtaagaa
15901  attattgctt ctctgttaat atgatgctgg tgctgaggca gctcaactga ctatacctga
15961  aatctcttacc gaacatttt aagtaatcgg ggacaggtta tttgatttcg ggatcttcct
16021  agatgtttgt tttcttcct tctgctgttt gcttttttcc ctcagtccct ctgctggagg
16081  gggacctaac acaggtgtgg gatgaaactg agcaggagcc ttctagctca gtgtgtcttg
16141  aatttccttt ccactgttct tgccaaatgg gcagaaagtg gcccccatct tagttttttct
16201  aatcttctgg cttctcatgt ggacttgctt ttgacagctg acccctgcag tgtggtatgt
16261  atagcttttg cacacgatgt gttcctctgt tattcttccc tatttttgat gtttatgcca
16321  tacagcgtga ggagtagcat caatatttct gatctggttc agtcagctta gctctgattt
16381  aactacttta tctctgcagg caatggtggc aattcaaaga cagcaccatc agcacactgc
16441  ttggcttgcc cttcctctgg attgccttca ttttgctttt ccaagtcatt tacctcatgt
16501  cccttctcct ccctgttctg taggattcta ctgacccctc tctcatttca tctgggcccc
16561  cagcctgtca aaacaaacag cctccctatc agcccttttct tgcagatgtc agcactgaat
16621  catacgatgac ctaagccat ctttgcatta tttccttatg gcatttttg ttttattgcc
16681  ttcctctgat actttccctа tgttaacct ttttgctcct tcactggcct gtgagatttg
16741  gctagacggg acttttcctg atttttgtat ggcttcccatg cccaggacag aaaatgctag
16801  aaaaacattg atggattact ctctttcctc tttcctacac ttggtctctg cattttтcat
16861  ccatcatctt ggatctaccc tgaagttatc ccctacttgt gcatagtttg ctgatctgct
16921  cagattttcc tgtgagagct gatttttctc acatagcctc tttttacttc tcagtgtcat
16981  ccactgtatt agtctgctag gggcaccatg acaatattcc tcagactggg tggcttaRac
17041  aacagaaatt aattttccca tagctctgga ggctggaagt ccaagatcaa ggtgtcggca
17101  ggtttgattc tcctgaggcc tctctcttgg cttacaggtg gaggttgtct tcctgggtct
17161  tcacaggccg ttccttttta tacacaaatc cttgttgtcc cttcctgagc ccaaatttcc
17221  tcttcttata agggtatcag tgagattgga ttgggaccca cccataggac ctcatgtaat
17281  cttcattact tctttaaaga ctttgtctct aaatacagtc aattctgag gtgctagggg
17341  ttagtgcttc cattactttt gggggtcata attcagccca taacgcccac tgactcaccc
17401  ctgctgtagc tggtagctgg agttcctccc ccagcctgtg taaactgatc ttggacttgt
17461  gtgaggctgc cctcaatgct gctcttgcag gaggcccaag acaggtctgt ttgttaacca
17521  tcctgtcctt ggaatctagc cctgcacaca ctagctacac ctgcatccac gctgagagtc
17581  ccaataatgc tcctgagccc tcgaatgtgc tgtaaaatgg taagagagcc acatatacac
17641  ttacaaatgg atgactccgg ctcatctgga cccctcctcc atctctcata gacttagaat
17701  cttttcggtg gttggtgggt ccctagagtc acatttatt ttagctaag gtggggtcac
17761  ttctcaccaa catttgcaag tgttcgataa gcaatgttac atctaaaatc aaatgagtta
17821  tagtgaattc tgagggagat gggcaggtgt tttataatat caaatattgt ttgaaattag
17881  caaatgaaaa actaatcaat atcttttgag cacttattgt gtaaggagca tagccaaaaa
17941  tataaaggca tagttccacc tagtttgaat tggatgagga ttaaagaaat tatgtatttg
18001  aaagtccctt acacatacag tactccaatt aacaagtatt atttcaccaa agcctttcag
18061  cccttagcca aatggaattt cttccttttt tttttaagta tagcttagtg atttaaaaata
18121  gggtttcctg agcttcaaag acctgtgttc aaatcttggc cttgttgctt ataaactatg
18181  tcacttttggc cagatgactt aaaccctatg catcggtttc ctcacctgtc aaatggagat
18241  aataatagta tgtacctagt agagttgtca tgaggacatt ggttataata acaacagcta
18301  acattagcaa gcagttattc tatgtcaggt attgctccaa gtgctttata tgcaaatata
18361  tgtattaaat gtatgtaata gatgtttcac ctcatttaat cgcttgctaca tggtctgtat
18421  taactagagt gggggctcaa taactccaag caatgccttt ctattgcaac ctgaagaggg
18481  agattagaaa tgtagaaacc attccattcat atctctccct catttaatag ctgaggacac
18541  taaggcccag agagtataat catttggcca agggtacaca gcatggcagt aggtgccaga
18601  gccagggcag agtcttccag gctcacatca aagggtcgtt tctgtggagc caggaggtga
18661  cattgggatg aaggaagagc tttccctcat ccatagggtt ctcaggtcaa acccacccaa
18721  accagccagg ttgtgggcct cccaaaaaac aaaaaaaaat ggtgtgaaac ctttaataac
18781  agatggtcca aacctgggga gaataagata aagctaacgg tagttacaga tgagacatgt
18841  tagtgtagga tttgactgca tgtggtttga ggacatgca caggcctctt gtcaactgga
18901  ttccacatac taaaggagtg tgctgggcag cccccgactc acaaacgggg ccatcagcct
18961  ttcctagcaa ggctttgttt cagaacttgg catgcatttt cctataaaaa caaggtggta
19021  acctgtgatt tggttctccc gccaacccac aaagccctgt ttaaccctag cagacctggg
19081  ccttcttatt aatggtggtt tcttattgtt tctttggaaa aatgcaatcc cagttccaac
19141  atgaaatccc gaatctggag aacttggcat caggctgtga atgaggcccc tcctcttga
19201  aaataattct ctcccctctg gccattccgg ccagggggtg gaggttcccc acacctctcc
19261  caggtccctt gatcagggca ctcagcggct gggaaacaag ggttggcata agtcagggat
19321  ccacttggac ctcaggaagg ccactgggcc agggaggaat aggccgggga gccacccacc
19381  tgagggaggc Rtgcaggaac ttagacactt ctctatttaa tttttatatt tcttctgtat
19441  tatctcccca acttactaat tttggaattg gaagcaagtt agtgaactтt tctgaacatc
19501  aggtttgtaa tttgttagaa gcgaaaatgc tctttatccc ttgggtggtt gtatagattc
19561  aaagggtaat agatagcaca ggagcagggc tcaggtctgg caaacagtga gtgactagta
19621  gaaaacctgt cactttctgt ccttaatttc catggggcta tgtgacatag tcttcttcag
```

```
19681  tcacgtagat aattggaagc tgtcagccta tcattagcat agaggctaaa gcacaaactg
19741  tggctgggtc tttgtccctg ctctgccagg acatggctac tacttcactt ccctgagtct
19801  cagtttcctc gtcataaaat ggggataata attatagaat tattgtgagg aacaaatgaa
19861  tacatatgtc aagtgcttag gtcagtgcat ggcactgatt ttgccattat gattattctg
19921  tatctttaga aaagagagtc agtgttataa ggcacagaaa gactaaattc ctagaaatgc
19981  tgtgacatta ataaaataac atcagtatcc agcaagcttg ggtgtacatg ctttcagtgt
20041  gtgtacatgt tatttatatc ctttcggcag tcttgggagg atggtagcat aggtggtatt
20101  cattattcca tattgcatgg ggggaaacag gctggatggt gaaatgactt tccttcggtt
20161  atgctgctag tcagcagttg agacaagacc acatcttctg ggttttcatg ctgtttttat
20221  tcctcaattc aacggtgttc ttaggtttga tttaatttct gctgggccg ggtgcaatgg
20281  ctcatacctg taatcctagc aatttgggag gccaaggtgg gtaaatcact tgaggccagg
20341  agtttgagac cagcctggcc aatatggtga gacccgtctc tactaaaaat acaaaaatta
20401  gctgggtgtg gtggtgggca cctgtaatcc aagctactca ggaggctagg gcaagagaat
20461  cgcttgaact gggaggcgga ggttgcagtg agctgagatc acgccattgc actccagcct
20521  gggtgacaga atgagacttc gtctccaaaa taataataat aataataata ataataataa
20581  taataatgac aacaataatt tctactggga cagaggagtc ttgaggggac tgagtctcgc
20641  agagaagagt gtgttcaggt ttctcacagt agagaatggg gaaccctatt cctgtgccac
20701  gttgtgtatt caggtgaagg gtgctgtggc cagctcttgt tttgcctcc agattggagg
20761  gtgtgaggaag tggtggctgg ggcctcagag gagggcctgg ggtgcctgtc ttcagtctct
20821  acggaagtct tgtcattgat ttaaaagctc ttccaagtta aaaaacaagc aaacaaataa
20881  aaaaccattg acagtctctt catgttcttg gcaaagaaca atttatgaat aattttatgt
20941  tcttgacatg ctctgaagat gaatagcaaa cacttctacc agaagtgaag aaatggctac
21001  taggaggctg agcttagga ataaatatat agtagattca attgttatct ttttttccc
21061  tcactctttt actggcatcc agcatttatt ttgaacttca gtcagaagtt atttcactaa
21121  gaacctgtgtc atagcttcaa catcttcctg aggctactga tatggtaact cggaagggggg
21181  aataatgttt gtagggccag actcatgtct gggtccaggg tctttcagaa tgttcctctt
21241  tcagttctca gaacaccctt gtgaggtcgg gagtatcatc gttactgaga agggcactta
21301  tcacaagtta ggcagtcaga gtatatttgt aagccagtag taagacagag ccgaaattgg
21361  agcccaaaca gttgttgaag aagtgcagga tcctcctcta ttttagtgtc actgaatatt
21421  tagagctaga ggaagagacc agagaaggag attttgcaga tgagaatcaa gcctatggca
21481  tttctacaga tggtcctcgg ggtgacatag agattttaga gttcatcccc aagtaggacc
21541  cggattcctg actaatgtga tttccccac tgatctgaaa gtgagctcag agaccccaga
21601  tatatgcatg gggagttcca gccctaatcc tcacttgttt gtgatggcca gctatcagct
21661  ccatttctaa gaattgtgtt ttaaagcaag tcacaattac tRgttttaaa aattcttcaa
21721  ggtatctgtt attaaaaaat atagacacac atttgggttt tcagctttgg tataaacttt
21781  tcttgttaga ctttgtaaca cctgacctaa ttgaacagtt tactgatatt ttctataaac
21841  agttactatga tattttactt ccctccagtg agaaatgaac gaatttcatc gagtgcagga
21901  ccaagtttac tttctagaac attacctata gaatacaaat gtttacattc caaagactgt
21961  tttattatgt aataagaatc atcaatttga catataaaaa tatgttttat tttgtaatag
22021  agatctttct atacattaat tacctctaca attttataga tgaaataggg cagcacaaga
22081  ttatggctaa aaaacagatt ttttttgagt gcatgcaaat caaatccaac ttaaaggaat
22141  ctgtgcaatt gacggcaaat agatctctct ttgtgcagtt cccttggagg tgaaaatgat
22201  aatctctgca tgcaatttaa ggcaattttg tgtgtgtgtg tgtgtgtgtg
22261  tgttttcctg gtgttttaga aagcctggat aaatccaagt taattttagt tgtagcagtc
22321  attccatcgg ttataggctt gtaatcaact cttagctgtg gtttgttcag atatttacaa
22381  tgaatgcttt cttgtatcta tacagtactg taaaaggtac tgtgctataa Ttttataagt
22441  acaaatgtgc ctaaatctga tatatttat aaaattcagt tggcagctgt gaaggcttgc
22501  tttgtctct tcctcccctg cactggctaa gtccttggaa tcagtatgtt aatgaagact
22561  tggtatctca atatgaaatt tgcaccatgg gagttctgag ataatgcgtc ctgatagagc
22621  ccctaatgcc tgcctcttag gagggcgagt gacaaagaca gtataactca gctaagtcct
22681  ttcataatca ggcagccttg gtcttttctca agtggttcca tagtttctgt gtgtgtgctt
22741  tcttgtgttt ctgtgtctca gacctcttct ctccttgggc agtctgtctg taatctttta
22801  atactgcatg gtagattgga ttggatgagc cccatcacct ttggataaga aaaggctttt
22861  ggacacaagt ccatgcaaca Ytcttttctt tagagaacac aatagatcac tgggaacatc
22921  ataagaggtg ctctcagagg gtgcttataa gtggcaccat cctaaatcca ggtttaccgg
22981  ggacagtctg ggtttataac tcatcctggc ctaatgaata atagcaccct cttttagcac
23041  agcatgattt agataagtta tatggtcacc ccatgcacat gggatgtggt agataacacc
23101  ttttaagaat aaagtgaaat ggattcaagt gaagtgactt acctacccat gtctagttgt
23161  gtcagatgga atccagaatt ggtccaggtt atcctggtca tttcaccagc taccccatat
23221  gctgtccttt gaaggaatta caatgctgg ctggttctct tttttaactt tcatgccaag
23281  aaacctcttt agtaaagtct tagacatttg ttgtttattt tagttggtaa aatacagcat
23341  taatttaaaa attacaaaat attgcataca taggaaggag tccgtaccct atgtagacat
23401  gatttaagta atgatgataa aacagacata gtgacagaag catatagaaa ggtgatcacc
23461  tgggaagggg tgcagagagg atggaaacat tctatgtctt agaatggtga gtacataggt
```

```
23521  aggtgtatgt atttgtcaga actcagtgaa ctctgcactt aaaatgggtg cattttactg
23581  tatgtaaatc ataccttgat acagtagact aaaaatttac ctatttacca ctatccaact
23641  taaaaaggag aacatttcca atacctttt agctttctgc ctggtgccga ttcctgactg
23701  acaagctgtt ttaaaacaca gaataactga ggctttattg ctaaatcaat gcctcctatt
23761  agaagactga tatttctgtt ttagtggacg ttctttaatc tttattttcc ttatttcgaa
23821  acgtcttgtt aaccctcttt acgtagtctt actcataaaa tattctaatt ctgtatttaa
23881  caagcggcat tttattttag tgatagaaaa aactgtggct gaaccaagtt ttctgggatc
23941  actggaatga tgttagctaa tggagtccaa tgttgaaagc atttgttgcg cacctactgg
24001  atgtcagaca ctttgcagac acgatcttat ttctcctctg agcctaataa taggtatcat
24061  ttcccttaaa tttcctcatg tgtagaattg aggcctatag atgttaagaa cttgcccaag
24121  atccccatgc aaaagtaatt aggagaatta ggagtcaggg tttgagcccc agggatctaa
24181  gtacattgtt aatgtagaga actgcccttt gctgggagaa gttaagcact tggctggctc
24241  ccctggttgt atcgtgtagc accaggacca tgtggcgtat cacttccaaa tttcctaaat
24301  cactgtgatc ctgcatactc cttgcccaga cccctcctgt ggctctctcc tgcttgccca
24361  ccgaggctca gctgcctagc agcagatcca cagggcctct ggtatctggc gccaacccgc
24421  ttatcctgct gggttttcct ctagctcccc tcaagggcct gtgtggctcc agctgccttt
24481  tccattagtg ttcccatatg ttccaggtta aggcctccgc tttgccttcg attgtacctt
24541  ttctgtcttc attgcacttg ccaaataaaa taaacaaaac aaaacaatga cagaccccag
24601  ctctccagtc cctgtcaagc agtcatctca aaattttaat tcctgcctct tctaggatgc
24661  cccaaatgcc agcctccctc tctgcaactc tactcatctt ttcatctaaa acagagttta
24721  taatgattga gttggtcctt aattgttctt taattccatg tctttttctt ctaataagaa
24781  taagaatgat aatagcttca tttattgagt cagatattgt gttctccact ttatgtggct
24841  tccctcagct aactcccaga gcaatcttgg gaggtaagta cacattttct tcccatctga
24901  cagactggaa aattgaggct cagagagaaa tgcctgagat cacatggcta ctaagtggca
24961  agactgggat tcggtttgac ttgagtttga ctactctttg ctgacttctt gcaaatgcct
25021  tgaggagagt agaaaagaaa ggaaactgac attgactgtg cctttgctat ggcttggcat
25081  cgagatggtt tagcttatta tctcacaggg tccttatcct gtgctaagaa tcagatctcc
25141  aaaaaaattg agaattagat ctctaaaaaa cggaggctct gtttacataa ttcattcaag
25201  gtcacagcgc tgattagtgg agagataaaa attaaaccag gtctttctgc ccctagagat
25261  gctccactgc gtgcatgagg acactttatt tctttttctt actctctgca tggcctagca
25321  tagagctgga tattagggaa acttttcaat tagttatagg ttgcttaaaa aacaacaaaa
25381  acaaaagttc cttttattct gttagaagca tgagcatatc acacatattc cggtagggaa
25441  gagtagtacc ataaagaatg ttggattttt agaagagaca acgtaaaagc aaaggtgagg
25501  tgagatagac acttgaacag aatggcagtc acagaatttc ttatcttttg agagatttac
25561  ttgagggatt ctacctttac tatagtagag gagtgtctaa aattaaaaga caggagaaga
25621  tgacttagta ttcccattca gatttttaaa ttgctgtgtg gttagctgtc tccagtcagg
25681  cagcttcact gctcctttct ttaactgcct ttctcaggca tagaagtaaa aagaagtaaa
25741  aggtaacggc cagttgccct cggcctctcc attggtggat ttgcagagtg ctgaaattca
25801  ccctagagtt tacccttcaa agtaactagg cattaaaaaa ctcataccta caaaaaagga
25861  actcctttgt gttccaacaa ttgttacaat atgttagact tttggtgatc aaaacacacc
25921  tccattaact gctccagcat cttgtgcatc tcagctgttt gtgcgagtca tccagcatga
25981  gggaggatgg gtctgcatca ggtgcagttc ctgggccttg gaatatgtcc tccacttttg
26041  tttgatcagc ggcgtgtttc cattgagtgt gctgtgtgcc aagagaacag ttgtcagtgg
26101  tattcgcagt gatgcacatt agcatgagtg ccagagattc aagtggcgac gagtaccaac
26161  tctgccttcc acccattgct ttttgtgctc tcagaaactg gagaaacgct agctttgcac
26221  actgggtttt ctcgaagcgg gctaggcgta tcatttccaa gggctgtgga gcttcctgga
26281  actgtgcatg ctgtgaacac tctcccagaa tgatgaaatg ccaaagtgct caagtcacca
26341  tgcctttgtt cactggctcc catgcctttc ttgctgtgac catccatgag gcttagaacc
26401  atcacagctg tttaggaaat ggtcttggag tccaacagac caaggtcaaa ttctggctct
26461  gtcacttagc agttgggtga ctgtaggcaa ttcatgtacc tctctgaact tctcatttct
26521  catctgtaaa gtaagtgaga gtaataacac ttatggggtt gctgtgatga ctaaaataac
26581  aaattctaag tatgtggcac ttggggtatg tgtgtgtgag agagagagag aaagagcggg
26641  agggagggag ggagagagag agagagacag gcaggcagtg gctgtttttt tgaacggcga
26701  tgcccacaga gggggagtta tttttggaga ggagggggtc ttctcactgc tcccaattct
26761  catccatgct ggggacgtgc atctgtctct gccactactc tgggaacata tctcttgtcg
26821  gatacagctg tctttctgtt gttcccttgg tctgccagca cagggctgag gccattccct
26881  gcactcctct tcctacttgt accccccactg caggccatgc ctggggactc cctgaccctg
26941  ctgtccttct cagcttggag cttgctgctc tttatgggga ggactttggt tctctttgcc
27001  aggctgcctg agaaacaggc ccaggtggtg tgaagtaata atccccagac caaatatgtt
27061  tatcgtctta tttgagccat cctgagactt actgcaacac tactttaagc ttagtgagtt
27121  taatttggat cacagcctat tatacatatg gcatggtgtc agcttttagt aaaagataaa
27181  ataggtgcgt gaaatgaaag agacatagat gccagttgga gaacagagtg atctaaaagc
27241  aaattctgca tagcaatatg aatacttcag agtggacagg ggtatagttt gaaagaagct
27301  acctataacg actgttttca ttatattgac taaagaaaaa aaaagctcga caaaatctcc
```

27361 ctaactcgtg gagtcatatg gaagatagaa taagaagaca gtgcacaatt gtgggcaaaa
27421 gaaggtaatg aaacattgca aagactttaa aaagcttttt ttaagttcta tattcacagc
27481 cacatttcgt aaacttaaga ggtgctgcat ttttttcat tcattcatcc atccagcaaa
27541 tatttattat ctagtgtgag taaacttgcc catgagccca tccctttcca ctgcctgtta
27601 ctgtatgtga caaggatagt agcgtgctca gtagcttgca accacgttgc ctgggtgagc
27661 gactcctcca tctactggcc cagtgacctt gggcaagttc cataacctct ctatgctcta
27721 gtttcctcat ctgtaaaaga gaaWtgataa tagcacctgt cacagagggc tttggggaat
27781 tgaaaatgca aggagtgcag agcaatgcct ggcatctgag agacattcaa tacatgttaa
27841 ctcttatcat ttgttttctg acttattcat ttgcttcttt attgtcactc tctctttcca
27901 tcattaaacg ctgagagaaa ccttgttttc tcttttctca tgtaactact atccttggtt
27961 cctaggacag tgtctgccca tggtagcagc ttagtaaata tttgagccga gtaagtgaat
28021 aaatggctgg atgaatgaat ggaatgcatg aaggctggac tctgtgctgg gtgcttccta
28081 gacaggagtg aacaaaactt ggtgcctgct gggtatatgc ccaaaggaaa gaaaatcagt
28141 acagcaaaga gatatctgca cccccatgtt tgttgcagca ctgttgacaa tagccaagat
28201 ttgaaagcat cctaagtgtc catcaacaga tgaatggata aagaaaatgt ggtacatatg
28261 cacaatggag tactattcag ccataaaaag aatgagatcc tgtcatttgc aaccacatgg
28321 atagaactgg acatcattat attaagtgaa ataagccggg cacagaaaga caaacttcgc
28381 atgttctcac ttatttgtag gagctaaaaa ttaaaacagt tgaactcatg gacatagaca
28441 tagagagtag aatgatggtt accagaggat gggaagtgga gggatgggaa ggaggtgggg
28501 atggttaata ggtatgaaaa atagaatgaa tgaaggaaca agatctagta tatgatagca
28561 caacagggtg actatagtca aatatatata tatatatata tatttttttt ttttttgaga
28621 tggagtctta ctctattccc cagactggag cgcagtggca tgatctcagc tcactgcaac
28681 ctccacctgc ctcgttcaag cctcccaagt agctgggatt acaggcacac accaccatgc
28741 ccggctaatt tttgtatttt tagtagagac ggggtttcgc catgttggcc aggctggtct
28801 cgaactcctg acctcacctc aggtgatccg cctgcctcgg cctcccaaag tgctggaatt
28861 acaggccact gtgcctgacc atatagtcaa taataattta attgtaattt aaatataatt
28921 ttacagtaac ctaaagagta taattatcct ttgtaacaca aaggataaat gcttgaaatg
28981 atggataccc atttatcctg atgtgattat tgcatgcctg tatgaaagta tctcatgtac
29041 cccataaata tatataccta ctatgtaccc ccagaaatta aaaattaaaa aaaattaaca
29101 ttaaaaaata caaaacaagt ggtgttgcct gcattttaga gcttccagct agtcaagtga
29161 aggagaagtc tagagatcta taataaccaa aggtgctaag tgtcaatgca agggaagaac
29221 ggggacacca tgctgtatgg catcaaggaa gaagtggcat tttccgacta tgttgagtgg
29281 tggactgata aacaagagca cttttttct ttatccatta gaagacttaa aataattatt
29341 tgtagatccc acttccccac tttttaaagc atttccttct caattattcc ctctcttcaa
29401 acatacaaac ttatacgcat attctaaaac ttgtaaaagg aagttaaaca cattttaatc
29461 atttaaaagg ttttttaaaa agtcaaccca tgtaacttaa aaatgattat gaagcacttg
29521 tttactttcg gttgtctggc atttatttgt gtgtggggtt ttttttttt ttttttttt
29581 ttggtgtatg ggctatttat tgcttttct taattttttc cttgtgtgtt tggaaagcaa
29641 aatccaaaca aagtcctttt tggcagtggt aataataaat attctgttta gcctttggat
29701 gaggtttaca tgatgtatct ataagcacat tctggaatat tggaataaca gtttccaatc
29761 cttttgatca atggatagtg ggataaatga aaagttccaa ccaaaatata cctactggac
29821 aagaaccatc atcttttaat aggcagaaat cctctttagg gtccagcctt cctttcattc
29881 ctgttctaca ttgtcaatga ctctgaccac aggaacagag aactgctgga tagggtgcag
29941 tgctgctggt cccctctatc atcaccagca caaataattg tattaatttt tttttagga
30001 gtggagttta agctcagctg tgcaccccag acattgatga agatagtcta tcgtatgact
30061 tagagtcaca gaaccacaag atgcgtgtgt gattatctaa ataaagagct cttactgcaa
30121 ccttgtgact ctggtgatag aactgggcgt gggagggctt tctcattcat gtgctgtgca
30181 cacaaatgat tctctaagtt gaaggacaca ttgctctgca gcataactga aaaatctgtg
30241 catgaatgtg tgtgtgtgtg tgtgtgtgtg tgtgtgtgtg ttgtgggggg gatgtggtct
30301 cattcctact tgcaaaaatc ctccagaagg ggttttcaaa gcattgcaca gctgttgctt
30361 gtcagcttct tgtgttgact agatgtcagc aacacttcct caactttgga caatgacttg
30421 aaagcaagat cagtgtgtgc tcatgggatg gatttaaatg gaattgaatg atacagaaac
30481 cattgcctaa tttatattta ggtaagtcat gtttctttc tctctctctt taaatttttc
30541 ctgaaatgca tgtatgaagc tctttttggc taaaatgaga gaatgaagca ggctcctgag
30601 tccttgagtg aagaggatcc attgagaagt ccagagggag agagaatgag cttgattaac
30661 ggcagcacag gattggcagg agtgatataa aatagtacat catctcagag tgacctaata
30721 ctcgactttg gaatgcattt ttatttttgg cagtggattt acctccctgt gtcctgcctg
30781 gacaaacgtt ggaattagtc agcattcctt aagcacatgc tgattatggc caaagaaagt
30841 ggcaggcttg aggcttgctg gcgaccagga gaaagccagc tggattagac atttgccgtg
30901 agccttttgt tcatgtaact tatggggcag tctcctaagc cagagaaaca agaaactcaa
30961 aggcagtttt agcaaggttc tcatgcatgg cagcatattt taatactaat gctcccttta
31021 ggcaggccct aaataagaat gtcttgttct aattttttc cgtagactta agattgttgg
31081 gaaaaaactt gttagaattc ccaagtgaaa ccatttaaat gccttggctt ctgataactg
31141 ggagtcctga gtgaagttgt cagttgctgc tgaactcagc agaaataatt gcgctcccta

```
31201  tgccaatgat ctgtgcatat tttgagacca ttctgagacc aaggaggcta tcacaacatg
31261  ttcacattgc tatcgttgat tagagccctg agctttacat gttgtctcct gtggtgtcct
31321  tcggaatatt ggagaggcat gcctctttcc tttcaatgtt ctcaacctgg cccagccagg
31381  attagaggct ccctctctgag gttcagtaga attttatctt taccctttat cattattcac
31441  cttactgtat tgcacttctc tgtctacagt ctccagcatt ccattacagt gctaggacta
31501  tgttggcatt tgtattcgtt tttcattact tcataagaaa ttgcccaaa tttggtggct
31561  taaaatgatg cacatttatg atggcacagt ttctatggat caggagtcca gacacagttt
31621  ggctggattc tctgccctag gtctcacaag gctgtactca aggaactggc tggggcttct
31681  ctcatctgaa gcttggagtc cttttccaag ctttcgaggt tgttggcagg attcggtccc
31741  ttgtgattgt ggaactcatg gtggcctttt ttctttcagg ccagcaggaa aaggtctctg
31801  acttgagggt gggccccagt ccttctttta ttttattatt atttttgag acagagttcc
31861  gttcttgttg cccaggctga gtgcaacctc ggtgccatct cggctcactg caacctccac
31921  ctccagagtt caaatgatcc tcccacctca gcctcccaag tagctaggat tacaggcaca
31981  cgccaccatg cctggctaat ttttgtatct tttagtagag atgggatttc accatgttgg
32041  ccaggctggt ctcgaactcc tgacctcaag tgatccaccc acctcggcct cccaaagtgc
32101  tgggattaca ggtatgagcc actgcacctg gccccagttt cttcttttaa aggcatcacc
32161  taattaggtc aggccccatc aacagttgat taaccttaat tatatttgca aaatcccttt
32221  gccatttaag atgacacaat aattggaatg atatcccatc atattcacag gtcctaccta
32281  tactcaaaag gtggtaggtt atacagggtg gatatagtgt tgaaagaagg aatgaatgaa
32341  atgaatgaat tctgatagct ggaagcacag caactagctt tttttgtagc atgagtgaga
32401  gaaggtattg agttccttat tgaagaatgc agttgcaaca gtttatcact agtgagctgc
32461  ttcttggtaa ctataagaca taagcagaca agaaacagca agaaaggaag gaaggagaaa
32521  agagaacgag aaggaaatca ttattttgga ccgatttccg gtgRtggttt caagaagttc
32581  tccccaccct ccagactgct gtcatttaca attgctagag aacaagagct gggagcctct
32641  cattggttct gctcctgtgg cataggccatg ggggatgcag aagggcagtg gtgcccaMta
32701  aagggaatcc ccgtcagctt tggttttagt ttccagagat tgagcctctg ccttaggctg
32761  agagaaaaac ttagtgtgag tctttatttg ctccctata atcacaggca catgtggcac
32821  ctcctcccc atctctgccc cacctcttcc aacagtgaga tgcattaggt gtggaaagga
32881  agccttcatt tcaaaatctc ctggctgcgg ttagctttaa aaatcaaatg gaactgtggt
32941  cgtctgtgtt taatttggaa gagcagaaag gatgcgtgct ttgtggcgcc tgcatagtga
33001  aagtctccat gacttaatac cactgcccag ccttagaagc ttcccatgca gacaatggcc
33061  ctgcttcccc atcagttctt gggcttgggt gccaccttat ataMacattg ctgctttag
33121  tgcatcgcag aagcaaaagg atgacacatt aatagcagct ggaggatctc attaaaattc
33181  Rgaggaaaat atgaaggctg gagcctggta atgtacagac agtaagtctt tgtctgtctg
33241  attaacaatt gcatgYattc taagtgcctt gctggatggt aagaaccagc atttcagcca
33301  gaagtaccat gttcttctcc ttaagaataa cctatttctg tttttcaatt cccttatccc
33361  ctctaaaaat aatatgctgg tctttcggac tccctgaga actgaaacag ctctagcaact
33421  ggggcagtcc ctgagagctg gtgcagaaac aactgttgct agcttggatt tgaattatgc
33481  agtcagatgc ttacatcgtg ggagggggat gtacgggggtg tgtggccttc agatgcttac
33541  atYgtgggag ggggatgtac agggtgtgtg gccttcatgc cagaaaggac agggaagcac
33601  tccctggttg gcgggaggag gggagatgct ggggttgagg cccttacctt tatttatgtt
33661  gttcactggt acagccagac tgcaacctct caactcttca gacaagacct aaggccgaca
33721  aaattcactc cctcatgaag aacattgggc tgtttctccc tggtgtgtag gtggtgggag
33781  tgaagtagag gggctcgctg tgtgcaggga aagggctgca ttctcaagaa tttgtatgta
33841  gcccttggac taaaaacaaa atattccaaa ggaatgcttc ttttggaacc ctggtccagt
33901  ccctcgtcta agcaggagtg cccttatatg cttgactgtg gatggcatct gattacgggc
33961  agaaggttgc actggattgc tgcctgatgc ggcacccacag aacacagttt aactctggct
34021  ctgtcagcag tcatcagtgt ttatttttcc aactcttcag agagatatta gtcgttatga
34081  aaagtgtacc atctcagaac tccatggaat aagctgccaa tataagacag gttgaaatta
34141  ttgtgtcttt ttgcctagag ttatttttag ttatttttttc ttccttggaa ttcttctttct
34201  ttttttttt taaccatata tgctaacttt gtagctggtg gcaaaaaaag attatttttcc
34261  ctatattaat gacttcttca gctgaattga ggaataggt taccagctct tttcttggag
34321  tttaacactc tcaatctgat aatatgaata acacctcaat aaccacaaca agagcggatc
34381  atcttcagta tctttcctga attaccttt ggctttttcac caccttgttt gtccgtttca
34441  gagtttgtct ttctgtaaaa tcatgggaag gcatctgatt actttgttct tgatgtacct
34501  gagtaatgcg aacatctgaa taattgaaca aaaatcttgt ttaaacaaaa ctttttgttc
34561  agaagcatct gtcaaattgt tagtcatctg acaatttaaa atgtcaaagc aagagttggc
34621  tgatcttaac cttagccttg tcacatttatt aacttcatgg agcttcagag taacttgaga
34681  agacttgcag tctgtacctg aaaaagccag gtttagaaag tggctcatga agaagtaaaa
34741  cctctcagtc aagtggaatg tgcaaggggaa cccctaggag cattttggca tgaacatttc
34801  ttttgagttt ctagcccaag acctcttat aacatttgtt cctctcccag ctgctcctcc
34861  tactgcctct aatttttaaa taagttctgt ttaactcatt tttggataat aagctagctc
34921  tgagaaagct tggtagaact attttcactg aaggagttct aaaactgatc atatctcttg
34981  tcatcaaatt ataacctgac tgttgcctgt tatctgaaat tctaagatag tgaagagagt
```

35041 tattttacct tttcttgtag ggcccttctg tcattacttc cttgctagaa tcctatgtgt
35101 gataatgagg gaatgaaatt atccaaaggg taatttgcag tatgcatcct acccagcagt
35161 tgaaactact gcagcgaaac tgcaaggaaa cctaacccat gttttcttgt aatgctaccc
35221 tttgggggtc atgcatgctg ctttctgctc caacagtctt aacgtgggaa tcggggacac
35281 ttactttttg acctggaaca aatctctaag actcgtaagc caccaattga ttcacctttt
35341 gtagcagggc ttgtatgaca aactcttttg tgagaacaaa aggaaagtcc cttccctttt
35401 tgccattctt gttctgtaga ttaattagca aagacgtagt ggagaaatgt gtcacttgca
35461 agacatttct ggcacggagt ggaccaagtg gaaatgctta aatgtgttgc agggatatca
35521 aagggactga gcttttggaa caaagaggaa cagagcccaa aggacaRttg gtacaaatta
35581 cacaattttc agttggttct aataaagttc taggaaaagg ggcttatgca caaaggctga
35641 gctcttgcct ctgttgttct tcaaatccaa aatgtcatta aaatactagt agtggttgtc
35701 atattttaat aacattttgg atttgaagtg tgtagctgaa acttactctt tgttaatgga
35761 tgtatcactg ggtgagcttc tagactgcct caccaatgga tctagcatta ccttggttaa
35821 tgaaatgagg taaaacacag tccctgtgta ccagaaagca ggttcatgtg tcagctgcat
35881 catgtcattt ggaactttgc aggtgtggtt ttccttgctt ccttcaatct cctcattttt
35941 ttcattgcct ggatgaagcc cctgcaacag gagagctttt gcctcctctg cctcacctca
36001 gccccctaga cctctgtgtg caactggagt atggtgttaa gtgagcctgg agcagtctta
36061 ggaaaaggct tcaagtgagg ctaggtggga aggcctggga cagaaataaa ttcaaaacaa
36121 caaccaaaga actgataggt ggaataaaag aagtgggaca gaaaagattc aaaggtggga
36181 attgaaagag agaggtacag taagaatagc tggcgtccag tgaacatgta cagtggacca
36241 tgcacagttc caagcacgtt cgatttatta tttcatctaa gactcacgag aactctataa
36301 gacaaaggtc tgacatttctc atccccgtgt tagatgtgag gaatctggag cacaaatgtg
36361 taagtaattt ttctgttgag aaatggacct atcaggggtt gaacccaagc agtttgcctc
36421 cagttaatgt ccttcgccac tttatattga actgagaaaa ggcgggacaa aagtcacaac
36481 caaaggtggc tttggccttc agaatattcc acctactgcc atcaatattc cacctttcta
36541 agcccacatg ctcctgtttc ttttttgtgc ccccaattcc ataattaatc atcctgcaa
36601 taaaagagac ttttggaaat tattttggga aaatgaagtc tttgggaggc caaggtgggt
36661 ggatcacttg aggtcaggag ttttaggcca cccttgccaa tatggcgaaa ccccctttgt
36721 actaaaaatt caaaaattag ccgggcgtgc tggtgtgtgc ctgtagtccc agctacttgg
36781 gaggctgagg caggagaatc gcttgaacct gggaggcgga gttgcagtg agccgaaatc
36841 atgccacagc actccagcct gggcggcaga gagagactcc atctcaaaaa aaaaaaaaaa
36901 aagaaagaaa gaaaatgaag ggtatagctg aaatctgctc atttcatgat cttgacaatt
36961 taaaaaacct gattgctgtt gcagtaggac tgtttaaaaa aggaaagaga aaaatatatt
37021 tttaaaaatc tgagcatgtt gaaagacaca aaggaccttt gttacaagtc actcctacca
37081 atggaagaac aaccgttgct ctcatctttt ttttttttt ttttttttgg tcatttcatc
37141 tctccagtgg ctgagatcaa tagagatgc tctatggttg ctttgagtt ccttggatg
37201 tcttaatgaa gggatgaaca tattgttttt ttttttgac acagggtctc attctgtcac
37261 tccctgctgg agtgcagtga cacaatctta gctcactgta gcctgacct cccgggctca
37321 ggtgatcctc ccaccttagc ctcctgagtg gctggacca caggcacgca ccaccatgcc
37381 cagctttttt ttttttttt ttttttttgt atttttagta gagacggggt ctcaacatgt
37441 tgcccaggct ggtcttgaac ttctcagatc aagccatctg cttgcctcgg cctcccagag
37501 tgctgggatt ataggtattc gccgctgtgc ccagccacat attgcttttg atgtagttaa
37561 acagttaact gctaccaagc tcttcacaga ggttactggg ctcaggaata aaaaggcttc
37621 tactccaaat ctggtagcac cttgcaccac aaagacttgc tctctcagta agaaaacaaa
37681 tggcagttct atatatagtc aagagtggag gcaggaaaag actacatttc tgaaaaatgt
37741 gttcccaaga aatccatgtt aatcaatgtc agagaccatc cagtttttat atattgcagt
37801 ctcaagaaat attctgccac agattctcta aggactgatc ataaaacaca aaacctttct
37861 atctttagta agtttgtcag ttctaacatt aaatgcttaa tttgacagt taccaaacaa
37921 agtcgattct agctttcctt ttttaaagtt tcaggtgaaa tttgctataa tctcatgtcc
37981 atcctcattc aggcatgctg aaagcactaa tattctgttt gcttttgagt gctaaagaaa
38041 tatagcccat gagattactg gccaaattga aaagaatgag gcttattgta ccaagatatc
38101 tttcttgata aattaagtca atgatctatt tcctgcacta gaggtcttga ttgggtatgt
38161 catagcgtaa ttttgtttgc cttctgaggc acacctattc tcttgctctt taacttggaa
38221 agctcctaac tcagaagcca ctctgtgaac atatggctcc aaagattgct tcagattcct
38281 ggctgcctgt gctaatgtca gtactcacct ttggacagga tatctaattt ttagattcta
38341 gacagttgaa agtaactaac ctctctaggt ttttcttctg tttcctagag taatagttat
38401 caatgtgatt taatctgact agattactat acatttttga acgtaatcat ttatttgtgt
38461 ttatattatt tgctctgtt tcagctacgg aatttttcta ttttttttt ttttgagaca
38521 gtgtgtcact gtgtcccca ggctggagtg cagtggcgca atctcgctc actgcaacct
38581 ccgcctctca ggttcaagca attctcctgc ctcagcctcc caagtagctg ggattacagg
38641 cgtgagccac tgcgcccagc caaggaattt tgcttttctt agtcagctag attttaaact
38701 ccacgaggtc aggaaactta cttttcacac gtttttcctt cttatagaat aatattttct
38761 cgatatgttt tagaggtggt attttatagg cagtggttaa agactgaaaa ctttaaccac
38821 tttaaactct gaaattctag gcaatgggat ttgtactgaa agacatagga taattatgac

```
38881  acttcaatta tagtccgttc aattcaccac tggggtggtt ctaagtttag ttcatggtgg
38941  ctttctccca ggaaatctaa agtactttac atatatagct ccattgtttc tcatagcatg
39001  caaccttaac ccagtgtttt cacatgtgat ttgagagctc gataccccaa ttatggtcca
39061  tgcaccagca gcaccggcat cacctaggag ctggtgggaa atgcaggctc tcaggcctca
39121  cccaaggcct catgaatcag agtctgtatt ttaacaagat ttcgggtgat ctgtgtgcac
39181  attacagttt gaagagataa gacaccaaag ttaactattt ttcctgttat cacatggcaa
39241  gtagatctcc agtcctgagt ctgggttgca tagcttgtga tgttgatgtt gcaaagatgc
39301  aggtgccttc ttttcccatg atgatgcaga gccccctcag ctcctgttgg agcctgtgat
39361  ggtctctaca ctccgtgttt ttcttcttag gctctttatc tgtacctgcg ttgcttttgt
39421  cccttaaggt tttgtccctt tgatttcctc ttaagtgctc tgaacttaat catttttttgt
39481  ttcttaattt taacatggcc atttcagtct gatgacagtt ttataatcaa aacccacatg
39541  caatcgatta ataatgtttt ataaagcaac agttgctacg aaaaaaagtg gatcttcctg
39601  agatgaggct atatgtaaaa tatggatgga atttgtatgc caattgggaa ctgatggaga
39661  aatgtatttt ggtctgacat aaaagttcct ttctcaaact actttcatac aactaagcaa
39721  tgaaagagca gagaattctc aactgcttc actactggaa agtaaaggga aatttatggg
39781  ggtaatagtg acattgagaa gtagttcttt aaagaactgc atttttcata ggtaactgga
39841  aacatttcca gctttgaaaa tgaacagata tcttttttctc tcatgtttag taaggcttta
39901  gaaatgagta ggaacaattt ggtagaattt cttacctgta tttcaaaaca tgctgagtct
39961  acttgttaag taagatgttt taaaagcatt tggtccttgg aattctgcta ctcataagaa
40021  tgcatttcta gagccgggcg tggtggctca cgcctgtaat cccagcactt tgggaggccg
40081  aggcRggcgg atcacgaggt caggagatca agaccattct cgctaacacg gtgaaaccac
40141  gtctctacta aaaatacaaa aaattagcca ggcatagtgg tgggcgcctg tagtcccagc
40201  tactcgtgaa tctgggaggc ggagctttca gtgagcagag atcatgccac tgcactccag
40261  cctgggcgac agagcgagac tgcatctcaa aaaaaaaaaa aaaaaaacaa aaaaacgcat
40321  ttctataacc tgcaccgatt ttgtagaaat tagtgtgatc tgaagctagt tgtcctgaat
40381  atgctttatg taaatatgtg tggctcactc aagtaatttt catctcttag attacatctc
40441  tcgatctttt tggatgtaac tggatttgct ggagttaaga aWgaacgttg tcattccccc
40501  tgcccaccc caccttcctc ggctattgat gtaataaatg taattacggt actaagaaat
40561  cctttccagc tgaaggaaca aaccacaaag tctgtgcttt aaatctttgt aatttttttct
40621  ttccgtttaa aatctaagcc atatattcag atttgggcgt gctttttgca ggtgtctatt
40681  tttagagctt tcoctgtttt gtaatttccc agttctcagt catgagtatt ggggaaaaat
40741  gcacattaaa attggttttt actttgttt tattttaaaa tttgttttga gttttataac
40801  tttaaaagcc tcgtgcattc ttttcacagc ttccagcccc aggaacatgg caatggaaca
40861  tgtttattgc cagtctagca tctagaaaaa gctaactcct ggatgacaca aagtaaatga
40921  ttgcaaaaag aaagagagag aggaagaaag gatgacaggc aggggaaaga tcagggggtc
40981  tgaccacaga ggtggcgcat tttactgaat taagcatgat agttgttgcc agtgaaggtc
41041  tcacgaggcg ccacatgtgg ggtcagagtt tgcctgtcac atgtggttgg cagccagcaa
41101  cagccatagc aaggctgagg ggagcatcat tcatttttcc attcagttag gtttttgttt
41161  ttgtttttttg agacagggtc tccctctgtc actcaggctg gagtgcagag gtgcaatctt
41221  agctcactgc agcttccact tccccaggct caagggatcc tcccacctca gcctcccgaa
41281  tagctggtac tataggcaca cgccaccaac acccaactga ttgttgtatt tttagtagag
41341  atggggtttc gccatgttgc ccaggctggt ctcaaactcc tgagctcaaa gcaatccgct
41401  ggcctcagcc tctcaaagtg ctgggattac aggcgtgagc caccatgccc agcttcagtt
41461  aatgtttatt gagttccctc cctgggttaa ggaatgatac ttcagcttta acagtgaggg
41521  gtaggcgcca ggatcaggtc ctgggatgtg tggctgtatt tttctggcat gagcagcttt
41581  ctcaggcatt ggttctttcc aagcaggaaa gtttattaga attttgcaca gatgcggttc
41641  atttcaccca ggattttgtc ttagttttag cagcagagac agtgaatctc actgggtctt
41701  aatcaggaga aggagttggc cgttaaatga cctcaggagt ggcttctggc ttagacccta
41761  gagatgccgt gtggtttgct aaggatcaac tagctcatga caaatactag aagagacttа
41821  ataaatctgg acctttcttt accaatccaa gttgcttgag ttgtaaatga tgtaaaaata
41881  gcaccctaca gacactagtt gttcagggtg aaatctctta tttccattag ccctgattct
41941  agagaagagt ggagagttgg ccttaggtgc cctctttgtc tttgactgta tatgtggcac
42001  actttcttca gccaatggaa tggcatacgt tgtatgccat ctgcaagagc ctgataagtt
42061  gcattacaaa tagagtgtgc aaacaatagt actgattaag tgacaaatgt tgaggcctgg
42121  gaactgattt ttggcactga caaattaagg cagattagac cgcctttcag gacacttttg
42181  ataatgctac gtgtatgtga aagaagaagg tatcagaaaa aacttaatag agtttcttag
42241  caagagtact ggaacataat tgtggatgcc taagaggaag tgtttgagtc aggaaaattt
42301  cagttgtcct gaattgatga acgagtctct ttttagtaaa tgcttctttt aacggtcatg
42361  gttagttagg acttagagac aaattacaga gtagcttatt gttatttctg ttgttgtata
42421  ataaacttt ggagatgaac ttcattaaat gcccctggtc tggttttgtt ggtgaaaagc
42481  tgaaataaat ctattgttgt taacatctgt ggtgatatag acttgaaatt atatctctag
42541  catgggttag aggagctgtg agaaacagtg aaaattcata tagcacttat tatacacagt
42601  gtatgaaatt aataatctct gcatcctcct cccaattgct gaaattattc ttacggtttc
42661  catttcattg tggtaccata gagtatgtaa gggatgctgg ggctaagact attagcatta
```

42721 tgggaatatt taaatataat ttaatatgag aaaaatcaga ggaatgtgca aactctaggc
42781 tgtatttctc cctaatgggt aaatccagtc atatatctct gacagaattg taaaaacact
42841 gagttatttg atctttcctg actgacttat cttggagtca tttatattta taacatgctg
42901 tgcaccaaag catgaaaagc agaagcatac agtttcgctc tcatctgaag taataaaata
42961 tttttattt acatagtcaa tctgggatag attatagtag aaaaccccta caaatctgag
43021 atactgaaag tggtagccgt tttcagagat aaataagtaa gcattatgcc tgattagatg
43081 tctttgctac tcacatggta aataaggcgt aactttgctt gtttactcct ttaaatttcc
43141 ttatagatgt acttactttc tttttatatg tttaaggtct tagtagaatt tcatcccttc
43201 ctccagcttt ttattgtata aaatgttaaa tgtggaaaaa ttgaagaatt tatgtagcat
43261 agcacatctg tatatctact acctaaatta attaattaac atggtgctgt atttcgtttc
43321 tctctctctg tctttttttt ttttttttt tttgagacag tcatctcgct ctgtcaccca
43381 ggctggaatg cagtggcgcc atctccgttc actgcaaccc ccgcctctcg ggttcaagtg
43441 attctcctgc cttagcctcc cgagtagctg ggattacagg cgcccgccac tacatccagc
43501 taacttttct gtatatttag tagagacggg gttttgccat gttggccagg ctggtctcga
43561 actcctgatc tcaggtgatc tgcctgcctt ggcctcccaa agtgttggga ttataggtgt
43621 gagcaaccgt gcccagcctg catttgcttt ctctatttgt gtgtgtatat gtgtatgtga
43681 aggtatgcgg atgtgtgtat atatatatat atgttttttg ctgaacagtt tgagattaat
43741 cagggtaagg agatgtcatg atgcttaccc tctctctcta tatatttttt aaggcagggt
43801 ctcactatgt cacccaggct ggagggcagt ggtgcaatca tagctcactg cagcctcgaa
43861 cttctgggct caactaatcc tcccacctca gcctcccaag tagctggaac tataggcaca
43921 tgccaccaca cctggctaat tttaatttta tttctataga gagaaaatctt accatgttgc
43981 ccaggctggt ctcagactca agtgatcctc ctgcctcagc ctcccaagta ttcagattat
44041 aggcatgagc cactgtgcct ggcctaagtt cttgagcatc tgtttcctaa tagtaagggc
44101 attctcgtac ataaagacac taacatttca aaatatgaaa aatgaacgat aatttttcta
44161 ttatatctgg tatccagtcc atatttaaat ttatctagtt gtctccaaat tgtcttttat
44221 ggcgatttct tcttcctaaa ttcagataca cagtgctcat gcattgcaat tcatattgta
44281 gtcctaaact cttttatgtt taatctagca tctagaacag ttctctcact ttttttttt
44341 ttttttttt tttgagatgg cgttttgctc ttgtcaccca ggctggaggg caatggtgct
44401 atattggctc actgtaacct ccgcctcctg ggttcaagtg attctcctgt ctcagccttc
44461 cgagtaggtg ggattacttg tgcccaccaa cacgcccagc taatttttgt atttttagta
44521 gagacagggt tttaccacat tggttaggct ggtctcgaac tcctgacctc aggtgatcca
44581 atggccttgg cttcacaaag tgctgggatt acaagtgtaa gccactgtgc ctgggatttt
44641 ttttttttt ttttgacatt gactttagaa agagaccagg ccacttgcct tggaggacat
44701 cccacatgga ggatgtgtct gattgtttcc tgttgaggct gttcagttcc tctcattcat
44761 gatttcctgt aaactggaag ttaggccaga agtttggagt ttattagttc agttaatctt
44821 ttttgggaag atgaggtaga ggagattaag aaaaagtcag tgtcatcttc gcagagtgat
44881 ttttctttaa accctggcct ctgtgatatt gagaaagtca caatattgga aggtgacact
44941 tgtcaacttc tgattagagt ctcttcctta ttttaaaaga catgaactaa aagttggactg
45001 ggttttcctg cctccccct tcaccctatc tctttctatc tcctcttctt tgctcttcca
45061 tggccatgag tatgtgccac taataggaca ttttcttaca atgtggcaat ttccttgtat
45121 acgtttatgt ctagcccacc attctatgag ctgctgacag cagggaggtg ttgctttttt
45181 tgtgatttct tgaaacccaa tataattcag tgttatcaca ggccaatttta ttaacattta
45241 aaactctctt cttggccagg cgtggtggct cacacctgta atctcagccc ttaggaggc
45301 taaggcagga ggatcacttg agcccaggag tttgaggctg cagtgagcca tgattgcagc
45361 actacactgc agcctggata acagagcaag accctatctc aaaaataaaa taaaataata
45421 aataaataaa agtctcatct taaatttgat ggggaaagga attttctgga tccacaactg
45481 aattgtctat gcttggcagg cagatgtttt ctcaaatggt gaatggattc accttctttc
45541 tctcctctag tttagctact ttcactccct tctagtcttc atatattccc aagtgaagtg
45601 agaagatagg tctgtatatc agtgactgtc cttttctttt Wtctttcga tttctcttct
45661 aggagctgag atgtttcttc tctgaacttt atttttcatt gcttatggct ttttttttcc
45721 cccctgtaag ttctctgcga gctatacacc tgtggaaata tagggactct ccttcatttt
45781 caaagagctc agaatatcgg tgagacaaag tcccttcctg cctggacatt cagattggcc
45841 ctatggactt aaattgtcaa gcaagtatac ttttttgtgt gccccgcaac ttggcctaaa
45901 ctttgctata aatggcaaag ttactgaatt gccttggctc catacccaat gttggaaata
45961 attttaggat ataaaaacac atctttcata tgaaagtatt tcttttaggg tccctgata
46021 agcatatata tgtgttactc attttcctaa tgaattagYt cctttcttca attgtaagga
46081 taaccctca ttaatatcta atttgttgga atgaaaatga ttccagtaac atttttatga
46141 cttcaatgtg actcccttat gaaaaggcat aatggaatgg ctacttttaat caaatttgaa
46201 gaaaaaagaa atatattct gaatacgcac ttcataaata ggaaaggcag ttttcagcat
46261 ttacttagg tatcatttat tcagtgagag cttgagggta accccaggt tcctgcaggc
46321 aattaagacg aaagtcatga ttttggagag ctctgggttt agtaaaacca cattagaata
46381 gagttcttag accaggaagg ggccctagaa aaccatcaga tcaagcctct tgcctttagg
46441 caaatagtgt actaacccct gttgacagac aagcatattt gaaaccaata atggtgtttt
46501 gaacaaaaga aaaatagggg cttggagcct gggttttcat cttttattgc actcttccta

46561 ctgtaattat agttttattt ttcaattcaa ttcattggat ccgagaggag ctcatttatc
46621 gatttgcaac ctaagtatta gccatggagt cattcttgaa ctttgccgtg gacttgggtg
46681 aaaaatgttt ctggttttca aggcttccct agtatcatat ggtattggaa tcaaaaatag
46741 agtattgttt taaaactgtc agcataggca gaacttctca tccagcaacg cattccgtag
46801 ctcaagtcct cattttgaac ataggattgc aatgctgagc cctaccatc tttccactgg
46861 aaggaacagt tgggcagctt tttaaggtac ggcgcctcgt ggaggactcc attaatgagg
46921 aatcatggtc tcctgacttt ggattgatca tttttgttca aaacaggagt attcctgagt
46981 cagagtcagc cacagcttat aggcaacaat tttcaggaga caacatccca agttaactgc
47041 ttatggcccc caaaactgta aggcttgtga tagtgcccca gtgaaatatg ccactgtggc
47101 attcccatcc ttttagctcc tggatttctc cttttcagcc cataataggc aagggcaagt
47161 aagggaacta acaattatat gagcacttcc tctgtcccac acatggtgct aagtccttta
47221 aagaaaacaa ggttttcttc actggttctc tatggccatt attagagaat gctggagtca
47281 ctgatctgga aaaacctgtt taattccttg gtctcaattt cttatctgta aaatgagatt
47341 aaattggtaa aatatgtgaa gcacttaaaa agtatgtttt aaatggtact tagtgttacc
47401 cacttcatat acatttctgc cagctctatc atacctaatc actcatttga tcatgtcatc
47461 ctcttcccag tctctgttct ttgagctgaa gaatgtttgg tgattcctgg ctgcttctgg
47521 gcaaaactcc ttagtttgtt gtgtgatctg gccccgtctt acctctttag actgatagat
47581 cccttcattc tcgcattggt attaaaaatc aatatagacc atgattttgg gtttatggct
47641 tctgtaagtt tgtgaggttt ctctacctaa aattccctta ccacctgtcc tcctatgtcc
47701 cttccctcta cagtctccac ctgttcaaat ccccatgtcc cttcaggaca cgggtcccag
47761 cctctgcccc aatgtagcct ttcctgcttg cctttaaact gggagtaata tcctcctttg
47821 gattactagc cctgtattta tagctgtttt gaaaccctat ggaagtgtag gctttgaatc
47881 atcaaaaagt attaagtgat gttcagtact tccatttact cagtactaaa gttcatcagt
47941 gtattttcaa acatttttca acaagacttg aaataaaaaa aaagtttttc cttaagaggt
48001 tttttctttc tttctttcct tttttttttt tttttttgtc catttgacat ctgaatcctg
48061 aattgactag acaaatttgg tttttctagt cagtggttaa ctgggacatg ccattcttca
48121 aacatttcta ggaatcccaa tacctagtag ctgattcggt cgtgctggag aatacaaagg
48181 cagtaatcaa agagcctaca cagagagaca ctgaatttta gaaccaggat aaatcaaagt
48241 gactttagtg aaacgtcacc acgatctgac gtgatctgaa taaaccacaa tctcagagag
48301 tgaggatatg ttttgagtaa atttgttctg tgtgttggcg agagtggctg cctagttaac
48361 cgtgggcagg tctgtgagtt tgcggcatgc cccttcgttc cagctgcttg ctgataggct
48421 ggcccaggcg ggatccatcc ttctgatcgc caggtcctga tgaggctggt gccaccacta
48481 catccattcc agggagactc ccaRtctctg tcagtttctt ctgcttttct gaattctaaa
48541 ctcactctga tctgatttca ttatttgtct gttgtggtag ctttggtgaa gttggaccac
48601 aaataatgat atagaagaaa aaatgaactt tttttcttct ttcctgtgtc cttttatcag
48661 gtatcatttc ctctataaaa ctaattttaa gttgatagag tcttaggtct atagccactg
48721 ttgaatgcac ctaatcaggc catctccttg aactagagaa tgtttgcatc ataggataga
48781 taccaggttc cctgagaggt gggtaccagg tgcctgggaa gtgaagtaac ttgccaagaa
48841 cagagagcca gggagtgaca ttgcaggcat ttaagcctag gcagtctgag tcccgaaaac
48901 aagtcaagac atttattgKc tttccatttc ttacccatgt tcttactgtt ttgcctggac
48961 tcctctttta atctcagtga aaaaaaaaaa aaaagtacat atttaacaac tgaagaaaat
49021 aaacagagac tgtagtaaat ttccaagcta atagcaagtt atgtaaaaaa tactacttgc
49081 tgatgaggtt tgtaagaacc tcctagaacc ttatagaaca agtgtggaat acttgttttc
49141 tgctaagggc tattgacccc aagaaaattc aatgaagcga tctttgcaaa atagtaaatg
49201 atttttcttt gtctccctgc agaagcaaag aggcttagac ctctagccac tgttgaatgc
49261 accaaatcag gccacctcct tgagctacac agaatgtttg cattatagga taggtgccaa
49321 gtgccctgga aggttggtgg agagagagat gacttccagc tgagattgta cagtagaatt
49381 taatatttaa agtttctcga tttgacgggg ctgaattagt tcatatgagt tcataagtag
49441 gaactgcttc gcttaatttt ggtgaataaa atatcctggc tgcaaaatac aaaaaagaaa
49501 gtcaccctca ttttcaaatg tatggttagt gctttccata gaaaacatat ggctaaatgt
49561 gtgtgttttt ttaatttagc tctgaaatgt gaagactgta ataagatcta gtaacaagag
49621 cgcagtttag aaaaacctga ttgactctag tttatgtaac tatacaggct atataaagaa
49681 agtctcataa atRaacttca tctaaagagt gtggcagcta taaccttctc caactttcag
49741 gctctgggtg ttctcctagc ttcttctgag tttatagtct ttatgtaatt attaatacca
49801 tgatgatcat tctggggttt gctttttgcc ctggtcactt taggtttaat tttattccat
49861 tcctggtcat ttaYagtttt gttctgtcat ctccccatac ccatcgagaa ccctattctc
49921 ctgtggcaga ctttaatgaa tgtaaccgca gattatgtgt tttctttctt tggtgaactt
49981 agaggatgca taggccaggt gccaagtgtt agaagaaacY ataccttccc tgatggtgct
50041 gcatggctag cctaccccga ccatgcagta agtgacttcc tcaccgctga tgtggcagac
50101 ctgctctgca tctccacagg gtttctgggt tcttttccag gctgtttcca tattgcacac
50161 tcagactggg taggaaagca ggcagggcac agttttatat gtacgtcagc attttcactt
50221 ggtgatggat ataagctaac ttttgtagct ctcctaggtt tattactgac atctgttccc
50281 ccctgagcat atccagctgg ggctgaagcc acatctgcac tttaaacttc catctacctt
50341 tatgttttca atgtaatttt agatttcatt tgtttttaat tgtgaactca gaagagatga

```
50401  gttccagcta tgactcagtg tgagttccta tgtcataatt ctacatttct ggagtgctta
50461  cacctgacag gaataaactc aaggaaacaa aaagaacagg aaaggcctta ggcacatact
50521  ggttgttcta gatgtggagt tctgctggca actgccacag agtgaaattg gccacatgga
50581  atccaaagca cggcctcaca ttgttttttt ttttNgaat attttatgta agacagggat
50641  gttaaaggta gaggaagtaa ttaagaatgg cagctatgtc tttaaaatta aacacatcgg
50701  tcataacttt aatgaaggYg taaaagtgtt tttagttttA aacaggcaaa aaggcttttA
50761  aatacaagta accagttttg agactttaaa aagcagaagt ttttcatgcc agtgcttcct
50821  attttagttt caaaggaaag gaggaggagc tgaggtttgg atggtatgca tagatgaggg
50881  agttgacatg atcaaaaatg ttttttccc tgggaacaca tcttgagtgc ttatctcttc
50941  taatagataa agggctggtg aattttgaat gtttcctgca gctctgaaga aacactgtga
51001  tcctaatgaa caccgaggaa agcttgtatt gcagccctaa atattacctg cttcaaggag
51061  gcagcatgtt ttggtacagt ctgatcatga ctataaatca aagcatcttt acttctccag
51121  ggagataaaa aaaatcatgt gttactttat aaggatcttg tagttgcagt atgtctgtca
51181  gatgtttcca ttttatgtat ttaagcacct tggtgctgct atgaatagca aattggaaaa
51241  attgggcatt ttttaaattt tgaatttTat cttagcatat atctggaaat gaaatagcga
51301  tcttggaaca gagacatctt tgttagaata tgaaagaatg tcagtgaatt ctaacttgaa
51361  gctacattga gatgacatgt taaaggcatg aatagacaaa gggaatgatt ttcaggaagt
51421  gcctttctgga gactgtggga aatcccgtca tgggtagagg aacagcttgc gattggatca
51481  aagtcacgca aagttacgca ggtggtagat gctggtagtc aacatggcta ggtccatggc
51541  aatcgatcat ttgcccagca ttttgcctgc tgaatttggg ggagtgaaga ggacattttc
51601  accaccccag gaagatagta actagtgctc tatgtatgta gctcagagcc cttgaatttt
51661  caagtgacct tttaaaagtt tccccagaa aggtttgaat agacttccta tctattactc
51721  taagtttagg tctaagaaaa ttcccaaatg ggttaataca gtcgatcctc aatctttgag
51781  aattctgtat ctgtgaaatt ggcctacttg ctaaaatgta tttgtaagcc ccaaatccat
51841  ccgtgaggac tctttgtggt cattggtgga tatgtacaga gcagcaaaaa aatttgagta
51901  gctcaaggta cacgtacccg gtgggagctg aacaaggtga cactctgcct tcttgcctca
51961  gttctcatac tgtaaacgag tgtcctggat gcagacaatt cagtgccatg tcttctgcat
52021  ttttggcctt tttcttggtg atttcactgt ttaaaatggc tccccaaata tagggctaaa
52081  gaactgtcca gtaggacttt ttttttttt agatggagtc ttactctttgt cgcccaggct
52141  ggagtgcagt ggcttgatct tggctcactg caacttccgc ctcccgggtt caagcaattc
52201  tcctgcctca gcctctcaag tagctggggt tacaggcatc agccaccacg cccggctaat
52261  ttttatattt ttagtagaga cagggtttca ccatgtcgac caggctggac ttgaactcct
52321  gacctcaggt gatccaccag ccttggcctc ccaaagtgct gggattacag gcgtgaacca
52381  ccgcgcctgg ccctgtccag tgtttttaag tgcaagaagg ctgtgatgtg ccttatagag
52441  aaaaatacat gtgttagcta agctttcttc aggcatgggc tttagtgctg ttggctgtga
52501  gttagtgtc aatgaaccaa caacttagat caaataagcc attttttttt taaaaaacag
52561  aaacacacat aaaatgacgt tatgagttgg ttgatgaaaa ttttgtgacc agaggctgc
52621  aggaacctaa ccctgtgttt cccccagaag ctaaggatta gtatttccta tgggtgtgtt
52681  caaggcaact tcatagacag aactaccatc atgaataaca aggatcactg tgtggctga
52741  gtgcggtggc tcatgcctgt aatcccagca ctttgggagg ccgaggcagg cagatcacct
52801  gaggtaagga gttcaagact agcctggcca acatgatgaa accctgtctc tactaaaaat
52861  acaaaaatta gccggtcaag gtggcgggca cccaataaaa tgacaataga gtttaaactc
52921  catggtttct gaggcatttt ctgagtaaat tggcatacag cgtatgtact ctttcctcta
52981  gaagttccag aaacaacact atttctttat gtgcaaaatg gcctcttttg agcagccctg
53041  gggcagtttt gtctggccct cttgcagcca gggtgcccca gtttagtgta caattggtat
53101  aaaaataggc aacacaggaa cttgcttgtc tcgggggaaa agacgcttgc agatttatag
53161  aaatttaca tttgtatgca tgatattctg taggttcaag aaaaaacaat tcaatttcaa
53221  gataactatc tacaggtaa ataaatttta atttcaataa attaaggggg aaaagttgtc
53281  catctttcta tactttctgt aacttttgta gtttcaccac taacaacaac aaaaaaaaaa
53341  gaacacaaac aaaatagcct tgctctgggt tttgaggaaa tggttttgca aggctatttg
53401  gttagacaat gaattagagt cagaacttcc gggatgggct ttcggtaagg gaaatgctta
53461  ggctgctgca aagcctggat tcaacttaca caggatcctt gagaagttgt tcttcgcatc
53521  cagaaccatg ggcaatgctc tatggtataa aaaccccgaa ggtaaacact gtctgatata
53581  tatttttttat aattgcaaaa tacacataaa cttaccatct tgactgtttt taagtgtgca
53641  gttacatatt cacattgtcg cacagtctcc agagctcttt tcatcttgca aaactgaaac
53701  tctgtaccat taaatgactc ttcatctccc tctctccagc tcagcccctg gaaaccacca
53761  ttctgttttc catctctatg aatttgacta ccctaggtac cttatataaa tagaagcata
53821  gagtatttgt ctttttagta ttggctgatt ttacttagca ttatataatg tccttaaggt
53881  ccatccatac tgtagcaggt gtcagaattt ccttccttct taaggctgat taatatttaa
53941  ttgcatgtat acaccacatt ttgtttatcc attcttctgt caatgaacat ttggggttgct
54001  tccacaattt gactattgtg aataatgctg ccatgaacgt gggtttgcaa atatctcttt
54061  gagaccctgt tttcaatttt tttttgttgt tgtatactca gaagtagaat tgctggatca
54121  gacggtaact ttatttttaa ttttttgag gatctgccat aatgttttcc atggtggttc
54181  caccatttta cattcccacc cacagtacac aggggttcca gtttctccac atccttgcca
```

```
54241  acatttgtta ctttcatttt ttttggtagc tgactgataa ttatgactaa ataatattgt
54301  tgaagaacta ttacaatgtc aagaaatttt ggccatcagt gatagtctta tgattaaact
54361  tagtagtatt ttattattaa acttagtagc attttattagt agtagtttta tttcagaaat
54421  atttgcattt tccatgtttc tagcccctca attatgtagg tagaaacaaa taatatagaa
54481  tcaatttacc ttatgttacc ttagaactgt ggccacagcc tagtaggtgc tcagttcatt
54541  tttgttaaat gaatgaatca atgaccatga agacagttca ggttatttgt tatggagata
54601  cgtaatggga ttggaaaaca tgtagggtaa atgtattagc cctctcctgt gttaactctt
54661  tagccctttc aaaactaaag gtatttggcc atgtgcggtg gctcacgcca ccgatcttaa
54721  ttttttatt ttaaaaatag cttacttaaa aaatagcttt gttgtattaa aaaatagcac
54781  ccagctaatt tttgtatttt cagtagagac agggtttcac catgttggcc agcgctggtct
54841  tgaactcctg gcctcaggtg atccacccgc ctcaggcctc ccatagtgct gggattacag
54901  gcgtgagcca ccacacccgg ccaggctttt taacatagta acataaacat ttttattctc
54961  acaatgtctt tatggtttgg gaatggtggc ttcctgtctt tcagagtctg gtgttatttg
55021  ttttttggt gtgtgcttg cagacacctg cacttgaaat ctttcaggta ttttgcagtc
55081  gtttttctcag atggctggat tatttcaagc caagaataac agagttaggg tcaagactgt
55141  gaaccgtatg gtcagtcctt ctaaggaagt atttattttt attcacttttt gtttgccttt
55201  ccttgggtca tggtcctaat tgctgttccc tttggctgca gttattcaaa actgaattta
55261  ctgctgagcc taagacagtg tttttcaaac ttttaaaatt aagacaccca gtaagaaata
55321  tgttttacag ttttttaca tcctgaccag atttacacac acacacacac acacacacac
55381  acacacacac agaacctgaa gtatttgttg caagttgcag atgtttacag ttactgctaa
55441  ggatatgtgt ttccatttaa tttacataaa atactgttca ttgaattgat tttatgactc
55501  acattatttc Rtcatgcagt ttaacaaata ctgagcactg gtgtcacaga actttgtcgt
55561  tcatgctctt tagcaacagt cagcttttct gctcatgact gatggcctat tgctatgatt
55621  ctgttagcgc tttaaagcaa tttgattgtc aaagtcatgt tagctctggt tgtgtattca
55681  gttactccagt ttcacctta caggcagctg ctccttggga aatgggggctt gctgagcagg
55741  ttgaatgttc catagaatca gatcttatct ttgggaaact cagcagtatg ggaatcacaa
55801  gccaacccac cctatccgtt aaagggctca ggcccattgg tctccattgt cacttagact
55861  agcacaacat cacctacctc atggatgctt tgagggcagg gccggttttg ttttttcttt
55921  tattcctcag agcccgcagc atgattcctt gtgtggagaa tatgcatcag ccttggctct
55981  ggtcctctct tcactgtccc tcttctcctc cctacagaaa acagcaaagc atgtatagaa
56041  agagatgtgc agactgtgtg gaatgacctg aggggtaact tgcttagagg gtagagactg
56101  ttgtgtgtaa aaacttatgt ttgaggcaaa ttgcaggaaa aagttcttta aatgaaggaa
56161  agataagatt ataagttttt taaaaagttg tcttaatgaa tagaggagaa tgactagtca
56221  ttatttcata gatcataggt acataggtga ttttaaaggt tgagtgactg gtcccttgag
56281  gttagttcaa tgtcccttg taatctgaat tttttcatca aattctttta aatccaggtg
56341  gggctcagct ccctctgaag tatcacaaaa ccctaaatga attaggttaa taagactaat
56401  tatatttcca tagcaatgtt taagtggcct gctgcccaat cacctctcaa gccctgctct
56461  gttgggtttc tttttaccca gtcatgatca cgtaggacca ggctgttttt cgtagggggt
56521  tatggagtcg caatgcctgg ggtgttagga atataggctg ggcttgtatc atagtaccca
56581  cgccgctgcc taactcttga tatccagtga ctgagttgga ctttgtagct gctttctctt
56641  tattaggaga aaagagcttg tttaataaac ctaagaatta atagcctgtg ttcagtagtt
56701  ggatttgtaa cctgaatgtt tttatgtcta ctgacttgca acgttgtcat ataaattaaa
56761  gatcatagat ccagctatgg tttaaaggtg acttccagga catggatttg aaagatcaga
56821  atttgaatct catctctttc cattctagct tggtaacctt gaggaaacca cttaacttct
56881  ctaagcctca aaggtgtcaa gtagattaat gcaactatgt atagctgacc ctgaggaatt
56941  tttggttccg ctagaataaa gcttgaattt ttggacatta gaaggatctt tgaagatgat
57001  gtagcttcgt tgtgtaactg aagaccagag aaatttaagt gagtttcctg gaatagttta
57061  tgcctctgct tcctgtgtca tgattaccac ccagaacacg tgcttaattg gggacaggta
57121  atccattcag ggtgaagaac atggcttttg ggtcagtctg cagtggatct aaatcagccc
57181  cctgctgttt actgtgtctg tagtctagaa aaagctattt aacttcttgc agattttagcc
57241  taactatgaa attaaattgg ggatttaaaa aaactcatag ggacgtggtg aggcttgact
57301  gagataaatt tatgcaaagc tcttagcaca atggctagta cccagaaagt gctcaacatt
57361  attattattt cctaattgaa gggcattgat gatttaaaat aaaatggagg ctgggtacag
57421  gctcatgtct gtaatcccta cactttggga ggccgagttg ggtggaacac ttgagcccag
57481  gactttgaga ctagattggg caacatggta aaactccatc tctataaaaa atacacaaat
57541  tagctgactg cggtggtgcc tgtagcccca gctactgaag aggctgaggt gggaggatgg
57601  attgagcccc ggaggtcagt gctgcagtga accatgattg tgccactgtg ctccagcctg
57661  ggcaacagag caagacccgg tcaacaaata catacatgca tacatacatg catgcataca
57721  tacatacata catacataca tgtaaataat taaataactc atttcttgtc agataaatgg
57781  ctgtatcttt ataataagat atctgtatcc tgtgacttca tcctgtaaat aatttgtgc
57841  ctcttgtgct ttctatgatc tagggaggag aaagctaatt cttcttcatt ttatgcacgg
57901  agcagagaca cggagagcct ctaatttatt tcttcttggt gtggccctgt tttctgagca
57961  tgggtgtgtc tgatccctgg ggagagcaga gccacactgt ggatctgagg tgctgggaag
58021  ccatccagtt tcctcctcct gaccctgact caagtcttcc ctgaaatctc tgtcagcccc
```

58081 attctctttc tgtcagcccc attctctttc tgtcagccgc cctccttaca taacccaaat
58141 gggttgtttg caaagctagt gtcgctgagg tgttctgtgt acaacagaaa agaatctagg
58201 gaggattcct atgtgtcact aaagccagta attaagtgga caacaggggg agctaacact
58261 gaatgcacca ataaatttca agactcctgc taccctaggt aaccgagtca atagtattag
58321 aaaccatttt aagcattggt agtttaaac atgctgttta aaaacaattt taaatttacc
58381 ttcactttc taattggata ctttactatt cagagtacta tgagatgagg gtctcgcttt
58441 ggagtgcagg ggactgatct tggcttactg cagcctcaat ctcctgggct caagcgatcc
58501 tcccacctca gcctcctgag tagctgagac tataggctcg tgccaccata gctggctaat
58561 ttttaatttt tttgtagaga tggggtctca ctatgttgcc caggctggtc ttgaactcct
58621 ggcctcaagc aatcctcctg ccttggcctt ctaaaatgtt ggcattatag gcgtgagcca
58681 ccatgcccgg ccaaacttct tttgaaatta gcttgttgat tcttcctcac ctcccagttg
58741 tttttgtgcc agaattaatt tttctccttg tattatagaa tagtttggag gagtattgaa
58801 agaattaggg ggtagagttg ccagatgtag caaataaaaa tacaagacac ccagttaaat
58861 gtgaatttca tataaataac tacttttttt ttgctataca tatgtcccat gcaatatttg
58921 agacatactt atactaaaag attgttaatt atctgaaatt cagatctaac tgggcatcct
58981 gtattttatc tggcaaccct aactggggtg gggatggtga ggagggcctt ggatgtggcc
59041 agaggagagg tgtcagagcc tcaggtgtct tcttgtgggt gaccgaggtg gctgcagcac
59101 agtagccttg ctccctgggt ctggggcctg tgccttctcc ctgtagtcac ttagaatagg
59161 atgatggggg tggctcaagg cagtggaata aattaattct gaaggaacac actgggccag
59221 agtcctagaa cagtttactt aatgatagtg ttattttaat tttcaattgt ttgcctttct
59281 tccctgtgat acggaataaa catgaaattg tatctggagc ggagcaggca gaacttacat
59341 cttgttggtc ttgttctgcc ctcagcctct gatgttctac aaggtttatc cttttgtttc
59401 tttttttatt atccaaggaa tgagatatgc cagaaaaatg tgacaggtat ttatgaaatg
59461 ctttgaacta ggtgagctta gagcataagt aatttaggt catttatctc atcacaacac
59521 tatctacaga gttttaaccc ttatcataag gaacagacca tgatgacact gacattatca
59581 acataacgac acacatgctt ttctattcct aatgctttgg tgagagaaac tggggcatcg
59641 gagaatgttc tcagccatat ttttgatatg gcctaaggta taatgaacaa aagcttagat
59701 gagaaaagtc catctgattg atgcctggct aattgacagc caattatgtc atggtgccag
59761 ttcttaaaga aattgaccca ttaatccctt tgtgtggaga ggccagccag caggcatctg
59821 ctttcttagc atgcagcagt actgaaaagt ttattgaaat aatcgtcacc tgtcctttcc
59881 aaatcttaat tcttctgagt ttaaacatgt tttctctaag gaaagtcgga ttgacatgaa
59941 atcacacatg tctggaatta tctctgagtc ctttataaac agaccaagac ttggaagggc
60001 acaccttagg ttacagagtg ttttcctggg ctgggctcca aagcttcctg actattgaac
60061 aataatgtgt tcttttccatg ctactttata tatttatttt acagaagcct tgtgcctttt
60121 atccgttcat atccactttg aaaacttact tgtggcctgc cagagcagag gtacaaaaaa
60181 ttccggatta ttttctgttt agaggcccca cacaatacag tatatgtgct gaagatgagg
60241 gcactcctcc tcctcctcct cctcctcctc cttcctatcc taccccttcc tccacctcat
60301 ttttcttctt ctttttaaa aataatcata agcatgtgtt ttcttctcat gtgcttgtaa
60361 atatttttgt tggggattct tgactgggat ttcagaatat cctgataggg agaagttggg
60421 tatttcttca tgagataaat tccttaagga gagatttgaa tagttttgac ctttgggttt
60481 tcttttctct ttcagttttc tttctaaaaa atgttacatt tcttggttat gagataaaaa
60541 caaacctata atttgtgata atgggtgaaa atgtgattag aattcacatt ctaggtttaa
60601 taatgacaga ctacttatga aagataagat gtcagagctg gaaggcttct tagatattgt
60661 cgggttcaat attcttttct cattagagga aatggagact cagagacatg aagtgacttc
60721 tccaaggtca cacagtaagt gagtgatgaa gctgggagta ggacctcttt tgcctgactc
60781 caaacacagc tttcccccaac tattgaggaa aaggactcag gacaatttaa catttcaagt
60841 cattgaaata tcctttaaat gctcaaactc taattttaac cttatgtgtg tgtgtgtgtg
60901 tgtgtgtgtg tgtgtataag tcgttctaaa gtacttaacc ttctgaaatc ttattttgac
60961 catgtagaac acagttcgac ctttttcaa tctcatcatt atcaacactg ttttgtgaac
61021 atgggtcatt gtggttttaa ttcatgggtg cccttgggct attctgagtc tataggactt
61081 gcccttagtt acattaacac tcccacatga caaaactcat gagtgcatgg ggaacttttt
61141 gatatccttc ctcattgtca gttgtcactt tttgctactt tcagaggtga tatttatagc
61201 atttcccccc ttctgtgttg ttcctaccca caggatttta acttacagag atgactgaat
61261 gatgacacag aggggacaag tccattgaaa taagtcttgt tttgttttgt tttgttttgt
61321 tttttgggac agggtctcac tctgtcgccc atgctggagt acagtggcac aatctcagct
61381 cactgtagcc tttgtctccc aggttcaagc tattctcccg cctcagcctc ctgagtagtt
61441 ggacttacag gcgtgggcca ctacgctcgg ccaatttttg tatttttagt agagatgggg
61501 tttcaccatg ttggccaggc tggtctcgaa ctcctgacct caagtgatcc tcctgcctcg
61561 gctggtgtgc taggattaca ggtgtgagcc acagcacctg gcagaaagaa attttttttt
61621 attactcaca tttcctaaga gaagagggca ttccatgcca cacagggcca ggaggagaag
61681 cacctatttg ggtgaagagg aagagatggg agtcagggga aagccgaggc cagagccttt
61741 actgggtttt tatggaaaag gcaaggcaga ctggaggaat cagcttgggg ttggctaggc
61801 gctgggatgg tctttagttg tcagttcctg gccctgagag atttagggca ggggaaatgt
61861 gggctgggta actgagagtt agataaggag gtggctcagc tagatcacag aggagatgga

```
61921  aactacttgg ctgttaactt gccctgtaat tgatggatac caaatagcca aatacagatt
61981  cggagaaaat gcaggacaac ttcccaggct tacttttgctg ccatttcattt tgtggtgaac
62041  caaaaaacca cttacacaaa cctgttggaa ggggtctctt ttgtgagtac tgtcaaagag
62101  agctatctag aagagacctt tttttgtgag tggtgaggtt taggctgaat ttttatttg
62161  ttttggtgct tttctgtaat ttgggattat taaaaacaaa gactagacct ttttatagat
62221  agaaacaagg ctcttttatt tggaaatacc atgtgcataa atgatgaata aatagagtca
62281  gtgaggacct tcttgccctc atgattcatt gttcttctcc ttctccttttt tctccttctc
62341  cttctccttc tctttctccc cttcctcctc ttccttcttc ttctttttta ttttttaata
62401  tgagacacag tctcgctctg ttaaacactt gtattagttt cattgaaagt gtaatataaa
62461  atctgaggat ctcagacatc ttaggaagat gactgtcatt tattatctat taaccaggtg
62521  agcaacttcc tggcgagtga ggggtgcggc agggaagggt ggagacgcaa aggcacagtt
62581  ccctttgtaa tggagagctt cagctcctgg gaaggatctg caatgcttag tggggctgtt
62641  catctctaat atagttaata attactgatt tgtatgaagc agaactgagg gcagggaggg
62701  atgtgggaag gccacaggag atatgagttt gcagccagag tttaccggtg atgaatcacc
62761  ttctgatcaa agcaggaggc tgggacctgt gggggatgca cttcgaccct ggggtgtgac
62821  ccaggaagtc agtgatttgt gaagggcatc ataggtcaca gatgcctttc caaagttacc
62881  agaacttggg atccaattta tttctcttag tccaggctca ggtttgattc ccaatccctt
62941  gcattcacac gagtcacagg gcagaaaagt gcagacgtgt tcttgtgcga cctccagatg
63001  tggtgtggag atggaagatg gtactctcat cattagagct gatttgcttt ggaattaaag
63061  agagacatac gcactgtgtt tctgtggccc atcatagttt ccactgatgg tgccatgtgt
63121  catttggggt aacattgact tgtatttcca ctcagtgtga ggaaaggacc ataagacaga
63181  attggagtaa tttctggaaa aaagaagtaa atgcttagta gagtgtcata cagtcttttа
63241  ataacaagta tttgataaac atgatttttgt tatccatcct tctgcaggaa aagaagccaa
63301  gttaattttc ctgagtttac agattggagg gttttagta taacctgtgc ctttttcctt
63361  cacctgttt cctcttttac tactacagta aagagggtga aattagttg caaaaggata
63421  ccattgaaat ttagttactt ttgctcgtct cttgctaaaa gagttaataa tgtgcagtct
63481  ttaacttgga ctgattttgg tataatgtag tgggtttcta aaaatagatt tctttttcat
63541  gtaattgaca attaactcca taagttactt tacagaaatt taagtttctc tagaaattac
63601  tgcagtacac attgcatgca ttctccttaa agaaaattga cagaacaaaa tttcatcctc
63661  tgttaggagc ttgcttttcc ctcacttgct catctcatga ggggaagcat gtattatatc
63721  atgtaattga cctcccgagc tgtatggcac ccttgagtga accaggtaca agcagcctcc
63781  acccaggcat tttcttaatg tccacaaagg ctcgctgact tcaagttagc tatttgtgtc
63841  ctttaacttg ttgccacaat ttaaaaccag gtgagcattt tctgcacaga gtggtcataa
63901  gcagtgtctg ttctgctgtg ctcggcctct ttgtcacctg ttcctatattt gggcatgaag
63961  cactaggccc atatgccttc accatttgc aatgttgttc tgggacagag ttatagggtt
64021  tttgccttga acaaagcatc tacattcttc atcttaggg agtgacagtt ccattgccaa
64081  tatgtggata tcagtttct tcaagcttgt gtatccactgc tatccactgc tgttcagttg
64141  cataatctct aagattaaaa actacatttt ggtaatgctg gcaacgaggg cacaaggaaa
64201  taaattgtct gtttttataa acatgtagct actgatattt ttttttgaag gtgaaagctt
64261  tatttaaagg aaggtctcat agagagtttt aaaatttag aatgaaaaaa ggtcttaaat
64321  ttattaacca aatagtaaac taattcattc aaccaaaaga cttactgaac actccctgag
64381  tgaaggtgtg tgtgttagga aatgtgctta ctgggtgaac acaacagagg tgttccccac
64441  ctcatgatac ccacagtcta gggagtgaca ggcaataatt aagtaatttt taaaaattta
64501  tagctgtaaa gtaaagcaaa ctatggcacg tccatgaaag agaggttaga gcctatgagc
64561  ggggaggcgg ggaccagatg gagcctgggc tcagggctg ccagacacac acagctgcct
64621  acgggcagga agggggccca ttggaagcgt taaacaagtg tctgtataga aggaaggcat
64681  gtgaataaag aaaaaagagt tgacctttgt gagttgtgac atccaaggtg tccaggaact
64741  agttttctcca ctttctttt ctccttttg tcatggccgg cagttgggcc cttgtactgt
64801  tcatcagctt caccatcaaa atcaaatgaa aagaaagaga agggagtgga atgctcactt
64861  tctagacctt actttaaatt ctgttgaaga ttttattaata ttttgggagag agtttgaaat
64921  gataatccaa aagatgtctc cctttgaaca tatgtagaag ttaatcattt agattaactt
64981  gcatttaaac acataattgt atgtgatcgt atacattttt tggctcactg ttttgtgttc
65041  aaaggcagat ttcctagggt agtgctgatt tattctactt cttttaggct gtgtaattca
65101  cctttttct aatttgggga aaattgtggt cactatagtt atatattttt tatttaaaaa
65161  cttgtaatat tttattaagt tatctaccca aatcttcctc ctgaaagata atatcttttt
65221  ttccttttt ttttttaat ttcagtaggt ttttggggaa taggtgtcct catagcttag
65281  ctcccactta ggagtgagaa tataggatgt ttggtttttc attcctgagt tacttcactt
65341  agaacaatgg tctccagttc catctaggtt gctgtgaatg ccattatttc attccttat
65401  atagctgagt agtattccat tatctatctc tgtatatgta tatatcacaa ctctttatc
65461  cacttgttga ctgataggca tttgtgctgg ttccatattt ttgcagttgt gaattgtgca
65521  gctataaaca tgYgataaca cagtatcttt tcagatatgt gtccgtctga catgttctgc
65581  accacccact acactgcagg gcatttaggt aagcagcatt tataagagtg actggaaatg
65641  gcttaggaaa aatggtacag aatgtaattt atcagaatca tcactgatcc tcttagcatg
65701  tgtattcaac aggtaactgt gactctaaaa tgttatttgg gagggaattt gcaaccaaag
```

65761 ttagaaacag ctctagaggt gctgggatct aggggcctta gattttttca tctcagttaa
65821 tcacaccatg ctttaggaag ctttaggata agattctggt gctagtgtcc ccggttggtt
65881 ttgcttctga gaaccaattt tgcagttgtc acatgatgag ttggatcctc atgcagatcc
65941 tccaagggtc ttactgaaca ccatcggttt atgctagtga gggtttgtgg ttctcagctt
66001 cccgcattgg aatgaacatt atttgggcct gagctgtgac agcttccttc ttcagcttcc
66061 ttccttgggt tcttctggtt ggggtatgga ccacttcttc tggagaacag cagggtggtg
66121 ttcaagcacc atcgtactct cctagtctag agctcagcca cccagtacta tagccaatag
66181 agatatttgg ctcaaaaaca catgagagat ggtagtgtga cagaataatg gaattgtaaa
66241 ttgtatttag ttttaatcaa aactttaaaa ttgatatcca atatatatga ttggaacaac
66301 ttgaatatgt gagcttacct tttcatctct aaagtttatg ataaaagatt tccagtaaaa
66361 atttaatgtc caagttgaga tatgctgtga gtgtaaaata catgctatat ttcaaagact
66421 tagtatttaa aaagaataat atacaataag taattttaaa atgttgatta tttgttgaga
66481 tgataatatt tttggtacat taggttaaat aaaatgtact attaaaataa tgttatcttc
66541 ttaaaattgt gatgactata aaatttgaaa ttgcataggt ggcttacata atgtttctgt
66601 tattgggcat tgccctagag ctaactgagg aaaagatcat agggcaccat ttgccattgt
66661 tgtcagtatg tggctttcag tactaggagg taaagtagat actctttcca tactaaatac
66721 taaatgccac tatcattaaa aaacaacatg gcaaatcttg cccttaaggg gacctcattt
66781 tttccccagc aaaacaaaac cgacagcctg ttatatagct aaagagtaga tgaaaatact
66841 taaacaatat aaatgaactt tattggttaa taggtgcagc aaaccaccat ggcacacatt
66901 tacctatgtg acaaacctgc acatcctgca catgtatccc agaacttaaa attaaatata
66961 tatataaaat aaactttatt agttatgcaa tgaaataaaa cagagcaagc aatacсttta
67021 ggttcactga attttaaagt taacaccttc aatacaaatg tatatatttt gtatacacgg
67081 ttatgaaggt atgaacatat taatgagcaa aataattatg aatacttgtt cctcttttgt
67141 agttttaaat atgtataagc aagaagtaac ttgacatgac ataatgctgt gccacccttgc
67201 ctattctgtc gtgggctcca aatgtaaatt catcagaaga gctcacagct ttgttgaatc
67261 tcctgcctct ttggggagat aggctcatat gtctcaattt tgaagcaccc ctcttggaat
67321 gaggtcagtt agaccactcc aaggaccact ctcttttctt ctttgtattt tctggggaaa
67381 acgtatagct agcatgctgg gactgtttgt tttgaatgag tttgtttatg agttttcaaa
67441 acaaaattat gaaaaaaagg gaagtttcca actccttgtg catgtcttgc tggctaagca
67501 gatgatctct aaaaacagat tacaatatca ttttgaaggt aacaaaggta tcttccttgc
67561 ttatctttaa ggctgcatat tttattgttt atacattggc caattaggaa ctgaaattta
67621 agaaagacag tcattttaac ctattgaagt cacagaatga aatgatgaag taatcgtatg
67681 tgttcccagt ttagcatata tgtatatata tgcattgatg aataatatga tttgttgtaa
67741 acaaatgaaa aactgcagaa acctgtaatt tgtacattat tatttcagat caccgtaaca
67801 aatattacca ggtttttaat tttctttaaa aaaatgcatt tctagggctg ggcgtggtgg
67861 ctcacgcctg taatcccagc actttgggag gccaaggcag gaggatcacg aggtcaggag
67921 atcgagacca tcctggccaa catggtgaaa ccctgtctct actaaaaaga caaaaattag
67981 ccgagcgtgg tggcacgtgc ctgtagtccc agctgctcgg gaggctgagg caggagaatt
68041 gcttgaacca gggagtcaga ggttgcaatg agccaagatt gcggctgcac tcctgcctgg
68101 tgacagagcg agaccccgtc tgaaaaaaaa aaaagaaaaa aagattttct aaaattgtat
68161 ttatactctc tgctccttcc ccatcagcca tcaacgcttc cctccctccc tctcccttcc
68221 ttaatgataa gccctcagct ttgctcagga ctcagcctcc catgtggttt tggtaagtgg
68281 tctaagacct gaggcccaaa gcgtgattgg ctgatgctgt gatttctcag cctggttgcg
68341 cattagaatc accctgggag ctttagaatc cagatgcctg ggctctactc acagagattc
68401 tgatttaatt ggtgtgttgc agaacctgac ttgagccatt tcgaaatggg tcattgatag
68461 cttgtagctg taacgattca aacatataca acataagcag ggtgaccaca gaagttattc
68521 tctaagtctg gtatgttcct aaatgtcctc taaattctta tcttccactc cagggctttt
68581 gaagtggcct gatccaaaca ccttctttcc gacattaaaa acattagccg gttattttgc
68641 ctcatcagca cttcctacac ttccttaggt gagccaggtt gcttttaatc tcttggagct
68701 gccttcgtta ataggccttt tttttttctt ttttgtttta aattgtatgt attgaaagta
68761 tacaacatga tatttgatat acatattcct agtgaagtaa ttactacaat taaattaaca
68821 cacccatcat ttcacatagt tacctttctt tttttgtggc gagagtacct aaaatctact
68881 atcatagcaa atttgtaata tataatgcaa tattattaac gacaatactt gtgtggtact
68941 ctagattttt tcatccaaga taactgcatc tttgtatgct ttgatctata tctccccatt
69001 ttccctgccc ctcccgatta tgccttttga ggcagtatag tgtgacagtt agccatcact
69061 gaattctggg ggccttttgt ctattccagg gagatgaaat tgttagagaa agattaggag
69121 aaagaatatg aaaaggactt agagaggata caaaatcatg aagtcacaaa tacctgccaa
69181 acaaatccac ataaggagaa aataaagaaa tgtcagattc ataaaagatc aaaaaaccca
69241 aactgttctt agagggaaaa gcatgcacag ttaaggaaac tttttttaaa aagttttaat
69301 aaaatctgat ctctagtggt aaatactgtt tcccaattac acctagactt ttatcgtgaa
69361 tcaggttttc tagttgacat tgttgttttt catttgaaaa tgaatgctgt gtattctcct
69421 tgtttcaatt cccttatgta tttttgtgtt aactccctct gccggggagc gccagactca
69481 gatgaaaggt attatgacat tcgagatgaa taatgacgta agaaggactt actctattgt
69541 atatcacggt gcagtatcaa aacattttgt cccatgagga gaggcagtga gtcagaaaat

69601 cctgttggaa ttgtattata atgtagaaaa ccatttcaga attactgtct gacatttggg
69661 cagctgggac tttgagctca ttccacggcc accccacctt agacatttta ttaggaagat
69721 gctattcttt tttagggcta tcactggatc tttgtcctca ctgatgaatt aattaggtag
69781 gtaataatga atctgagtta ttactgctga caatttagtc ttattcttaa aaacgttcat
69841 ttcatggtgt gttactctgt tctgtgttgc aataaaggaa tacctgagac tgggtaattt
69901 ataaagaaaa gaggttttat tggctcatgg ttctgcaggc tctgcaagca tggcaccagc
69961 atctgctccg ctacctgtga ggcctaggaa ccttgtaatc aaggcagaag gctaaggggg
70021 agcaggcaag acacacggcg aaagagggag caagagagag caagggagga ggggccttgc
70081 tcttttaacc aaccagctct tgtgtgaact cagaatagga actcacttgc tatggcaagg
70141 acaggaccaa gccattcatg agtgatccgt ccctgtgacc caaacgcctc ccactaggcc
70201 tcacctccaa cattggaggt cacatttcaa catgagattt ggaggggaa aaaacctcca
70261 aacctcatca catggttaag tggcataaga tgcaactcta ggaatttttg ctttttttaaa
70321 acccagcttc gagctccctt ccattccttc atcaagatat tcatgatgga tctgcattgg
70381 gacctgcttt tgtcttattg tttcccaaga ctaaaaaggg ttttcagcgc aagtgttctc
70441 gtaatgtttt tgtccccaag attggatgtt tttcagttgt attatctccc catatttctg
70501 acatgtacag acgtgcccag ctatgataKt ctgtgtggat ggtcttaaaa atgagttatc
70561 attatgaata gtttgatgga aagatttccc aggaagcatt atgctttgag tgttggggaa
70621 gagaagccac cagatgtcgt gtaggccctt gtccctttac tgcctttcct ctctgtttgt
70681 accoctgtac aaggcagctc ttgtggttac gatttgttaa caatttgagt agctccctta
70741 tattttgctt ctagagtaat taaacattgt ttcttagaaa tgtaaacatg ggacttagaa
70801 ttacgatgca gtaatgcatt tggcagctga actgtgtact gggaaaagaa aaatatcctg
70861 gagcgggttt aagtttcgca gataagaaaa atggctttat ttagtgaatt ggaacaatac
70921 aagacctgtg ccctgaagtc agtactttct cttcccagat gagtttcccc aggcacaaga
70981 ccaacttcta aaataaaact tgaaagtaaa tggcaaaaac cagaaacaga gccctgtaaa
71041 ctagactttt atgctacggc gccataaaaa taacttattt gctatcaaaa taagcttaaa
71101 cagaaccttt gtctgacaga tgacttttcc tctcccctta acctgacagc acccccaacc
71161 cagtctttgg tcataagcct gacagcacgg tgagatacaa gttcctagtg gcagtggagg
71221 ctgatgttta ttatttagag agtttctgaa aatgaaagtg taatgtcttg agtcacttac
71281 ttccaaattc ttcccagaga actttaaata gtgttgtatt aaaaaacagg agtaaacaat
71341 cattcgtaaa acacacccca gaataaatct cttatttctg catgaaggca actgatctga
71401 aacatttttt ctatgtgcct tttagagacg gcaccaaatt tcatgcgcgt tcgtgtgaag
71461 agaccaccaa acaggctttg tgtgagcaac atggctgttt atttcacctg ggtgctggtg
71521 ggctgagtcc gaaaagagag tcagcaaagg gtggtggatt atcattagtt cttataggtt
71581 ttgggatagg cggtgaagtt aagagcaatg ttttgcgggc aggagtggat ctcacaaagt
71641 acattctcaa gggtgaggag aattacaaag aaccttctta agggtggggg agattacaaa
71701 gtacattgat cagttagggt ggggcaggaa caaatcacaa tggtggaatg tcatcagtta
71761 aggctatttt tacttctttt gtggatcttc agttacttca ggccatctgg atgtatacgt
71821 gcaagtcaca ggggatgcga tggcttggct tgggctcaga ggcctgacaa taacacagtg
71881 ctcaaaactg tcagatagcc tgtgtcaggt ctgaagatgt gattttggtt gtttatactt
71941 ggatgctttg gatgggaata gccctggagt cagcccttca tttcaggcag aggagcagag
72001 gagtgtgagt tagacacaac tttggatcag gggccaggaa aacttggttg tcatcctgga
72061 ccagttacta actcgctgtg tgggcaagtc acttcatttg tctaagtctc tctttttcct
72121 tttgtaaaat aaggatgtcg gcaaatctgt gtggtccctt ccaacagtgt tttttaagtt
72181 ggtgcctgag tatctgaagc aggagatacg aagggtcatg tgagctgcac attcctattt
72241 gctccgcagg gaggctggct aagacacccg gcccctgcct tgtaaccatg aacaaggttc
72301 tcgcaggggc tcgtctcaac tgcaggtccc ctgaaggtct catccttttc tttgctagag
72361 ggaatttgga tgtcgttggt ccttgcctaa cccttgtctt tgaaagatac agatccaatc
72421 tctgtgtagc agttaagtga tctgactcag acatatttac tcagtcttct tagagaatga
72481 gaaaactctt ctcagaattt ttaagaatgt tcctgaagga caataaaagc tctcattcag
72541 gataggcccc aaaacatttt tttctttata atgtggtgcc atttcctcat tttgcttttg
72601 ttcatttgtt tattccttca acaaatattt ttgagaattt gctgagcact aggtattact
72661 agatactagg acagtgagat aagtaagata cagcccctat cttcaataag ctgtatgccc
72721 tgataatgat acccttagtg tcttctacaa gctatacggt catgcatcac ttaacgacag
72781 ggacacattc tgagaaatgc atccttaggc cattgcattg ttgtgtgaac atcatcgagt
72841 gacttacaga aacctagatg gcgtggccta ctgcacacat agggtatatg gtgtaaccta
72901 ttgctcctag tctacaaacc cgcatggcat gttaccatac tgcatactgt aggcaatttt
72961 cctctccccc taacctgaca gcacccatta cctgacaaaa atggtaagta tttgtgtatc
73021 taagcatatc tagacataga aaaggtacag taaaactaag gcataaaaag tgaaaatggt
73081 acacctttac agggcagatc catttacgca accaccactg catgcgtggt ccattgttaa
73141 tggaaactgt tgtgtggggc ataactgtat ataaaagtat agctacttta atttaagtt
73201 aaccctggta tgtgggaaaa tttgtcttct gtgctgtctt gcactgaatt ttgcattggt
73261 atttttccct taatagtggc tgcaaaaaaa cttataaata cagaaccttc ttcatttata
73321 gaattcttct gcattgacct ggaaaatgac gttgagaatt ggacgttaca ctacaatgta
73381 gtcctccaat gaaggctctc aatgggcatt tctttaaggc ctaagttaaa gataaaatag

73441 aacaacttcc atcactacaa aagatagtgt actcggagga acttgtagag attttttttt
73501 tcttgtagct gtttttctca ctactcaggt ttccttttg agttttgccc ctggaggctc
73561 agagttgaat tctgttggta gtcacttaga acttttctac tgctctgtct ttcctcagtt
73621 gtgttttccc catgtgggtt tgttttggga aagcagtgga ggggaattcc tttaggttg
73681 aaataacttt tagagcgatg gtgccacagt ttacaaatat ttttagaaaa atcctgtcag
73741 attcttggga acttcagact aacttcacat ctaaagttct cttttctttt cttttctttt
73801 ttccttcctt ccttccttcc ttccttcctt ccttccttcc ttccttcctt ttttttggtt
73861 tttgagacag agtcttgctc tgtcacccag gctggagtgc agtggcacga tctcagctca
73921 ctgcaacctc tgcctcccag gttcaagtga ttctcatgct tcagcctccc tgagtagctg
73981 ggactacagg taccctccac tacgcctggc taatttttgt attttagtc gagatggggt
74041 ttcgccacat tggccaggct ggtctcggac tcttggcctc aagtgatccg cctgcttggc
74101 ctcccaaagt gctgggacta caggcgtgac ccaccacgcc tggcctaaag ttcttattta
74161 aaaatttttc ttctgatttg ttagtttaag aaggtaggtt tgaagcagtg accaggaatt
74221 ttcgggaaat ccattaagga atgaattatt cagtaaaaca gtctcaaagt gaggggccaga
74281 gtgcaggaca gaggcagaga gagatggtag cagtttataa agagaagata cttgattaga
74341 gaaatcattg tcagagtaac cttatgctta gaaagaaatc acacgcgaag ctctgtgttt
74401 gaaatcagaa gggaaggtgg gcattcggat gaagaggctg tcggacttgc attactttga
74461 ccactactgt tgtttttgct gttgtggtgg ttgttgttgt ttggaagatg gagtaaattg
74521 caagcctggt ggatttcatg tgtttagaat tgtagctaaa atagctcctt acgttgaagc
74581 atttcctcaa ttctataccc acgttctcag tccttgtgtt actaccagta actcattttc
74641 caaaatgcag aattgcattt tacatttag ttctttcaat atttggatca aatacatgtt
74701 cagtggaaag ggtatgttta atttcctttt ggttcggcac taatttaaat tatgaataga
74761 gataacgtaa ttctagtatt cgtatttgat tgttaaaata tttggactca gaagtgcatt
74821 tacacgtttc caaatttgac aagtaggaaa aggtatagag tccaaactcc ttcccaggcc
74881 tatccacagc tacccagtgg cctatcccca ggcaaccagt gttaccagtt tcttgcatat
74941 ccttctgcat actaccaata caaaagcatg ttattctgta gccccagcta cttgtgaggc
75001 tgaggtggta ggatcactcg agccgaggag ctggaggtag cagtcagctg agattgtgcc
75061 actgaactcc agcctaggtg acagtaagaa cctgtctcaa aaaaaaaaaa aagcatataa
75121 tttgtttctt cttgttttta tgctgatgag gacatgctat gtccactgtt ccatggtatg
75181 tgccttata ttcagttatt cactaaaaaa atgagaagta tagagtaaaa tgaaagtctg
75241 tagtattctc cactagaaac aggtgtgggg ttcaagggag agtgtgtatt aattattgca
75301 aaacttctgg ttaggtcatt aatcagaacg ggagccatgc agtggtgaag ggccctggct
75361 atgatctgaa acatttttct gaagcagtgt tgagttctgt aactgaagtc catggggact
75421 tgctattggc ataactatat gtggaaaatt ttgcttttg agtaggacat tcccatgctt
75481 cacatttaat ttgaattttg gtatgactgt actaagttaa catagctttt cgcattttac
75541 agagacattg agtaaatcat tgactaaaga taattaactc ctttatatca Tatgctgaaa
75601 tgttatgggg gactatcact taccttctt ggcttatgga agagatgtaa tctaattcat
75661 tgagtctgac tgtgtttaag ctattgtttt gggtgtcatc gttggctctt agaacaggga
75721 ctgggcctta gtcctttcc ttgctcatac ctggcctcct cctagaagac cctgcttttc
75781 atgttttatg cctcagaacc aagatgtttg gggtcccaaa gtagggatgt gtatgagcac
75841 atttttgat actttcatct ttctcttact ctctaacatg cttcacgcta gtgtcatgta
75901 aatacagtga atcagatatt tctctgcctg caaaatgcct tttgccagta tgtgggaggt
75961 gtgttgcagg taccacagtg gattttctgc atctgttcat acatccatct ttcccactta
76021 gctgtgagtg gcctcagtgc agaatggtgc cttaactcta gagtctggta ggaaatgcca
76081 tgcacatttg tcaaatgaat ggaaatgcag ctgacttgct agaactcagt tctgagtgca
76141 gggtgcttga atgctatata atcaagttga gatcttagtc tggggcagca gaaaacaaga
76201 aaaggttact gagcaggaga gtgacaggct ttcatttgta tcttaatggg ttaattgcag
76261 tggcattaga aaaggggaga gattgggtta aggcattagt tggaaagctt tgatagaagc
76321 taggtgagtc aggaagggt tctgcattgc ttgtttccca ttgctctaac tagatttctt
76381 agaaaaaaga aaatcttaca ccagactttt acagcgtttg caactgagta aatttcactt
76441 tgtaatacc tggatattat acaattatat aaagcgcagt ataataagag agttagtagc
76501 ttcattgtaa tcagtaaaaa taattttaa gacaattgtt atttttgta tattgtatta
76561 taacaaaaaa gaagtcatca agtgggagga ggtgttgttt tgagacgttt gctttcatct
76621 cttaatcctg cagacattta tctagtccct tctctgtact cttaaatgct agggatttaa
76681 aagacggata agatacaggc ttattatgtc tgtgttccag acactggact ccaaacataa
76741 agcaaacatt acattattct tccttatgta atagaaatgt ttatgtaaga ttgtgtgtaa
76801 atcagtcttg aataaactga attaaatgga atgtgccaat aggagttgct atttagagaa
76861 gccctgtgat aaaacatttg tataataata tacttatcta aacaagccca ctaatttcta
76921 tgggttttt ttttttttcc ccccaaggcg aggtatcctg tatatctctgt gttgattgaa
76981 ttccagttgg ccaaccacct gcctggttaa tagagtatac cattaactta gtgacactag
77041 aaccctgcaa aggaaataag acacaatcta tcgttgttca gtctccacta ttaaatagat
77101 tttcattcac ttcagcttgg gtgggtgtaa tttgcatctt tcctaacagg caagcatctg
77161 caagtgtatt gcctgtagaa gctcattaaa aatcagtgca aatcctgaca ctgtctctag
77221 aagcaggcat taacttgcag aaagtggttt gtatttccag tgtcaKtaga gcttcctcac

77281 tcttttcctg cttccatgca agtttagtcc taaactagta ccactatttt agtacaacta
77341 gtaccactca aataatgctg cttttaaaat aaattcaagg ggaactgcta aggaactgag
77401 aacctgtaag gtgacaggaa aaaggaaatt ctatttttttg gggctagttt gtgtattgaa
77461 aataatttttt gctgagaatc aagctaagaa aattacttgc taatttaaac aacatgacag
77521 tcctcagaat tttccagcaa cagttaggag cactgtgata aagttggctt ttctgttgag
77581 aacgttttac ctttttgctt cagcttcttt aaagagtttg aaattagtaa ttaccagtaga
77641 gcagctttgc tgttgcgtcg tactgctcag agcttagtga gctgaagcct tttgggaaaa
77701 tagcatttgg ggagagactc gtggtgtaat agctcatccc actggcacat gtcccagagt
77761 aagctgggct ggaagctttt agtgtagtta aaagatgcca gtctgtcatt tgcatgcact
77821 gtaattgggc aagtggtttc aggctgagct ttacattatc cttccactga gagcagctgg
77881 tggtgggctg tagattccat atgagctggg gacttatcat ctggtgtgtt tagtgcaatc
77941 ctgcctcatc ttgggagcaa ttttttattg aatgataata ataatgcaca atcttggtga
78001 aagataatgc ttgtggttat tagaatgtgt agactgagta ggggctttgg catagagatg
78061 gtaatggtgg ggaaagacat atttaataaa aggattgtaa tggggagaaa gtaaatattt
78121 tgcaggataa ggaaagccac aaatatgatt aatttaagag tcttaaataa aatgtctata
78181 aaatgttaga ttttagtac cagtaaggca aagtggccaa tctctagctt ccctttataaa
78241 gtctactcat ccttggaggg tcgcttttttg gtgcttttttt tgtttgttca gagtcaactt
78301 cttcctctag ggatatgttt aagtctgtca cctttccttta ggaattgtgc caatctgatc
78361 atttgttcca ccactgctgc cccgcccct tttcttgact caaagaataa tttgtgtacc
78421 ctgtctctgt ttttttttt tttctttttc tttttttttt attatacttt aagttctagg
78481 gtacatgtgt acaacgtaca ggtttgttac atatgtatac atgtgccatg ttggtgtgct
78541 gcacccatta actcgtcatc tgcattaggt atgtctccta atgctatccc tccccctcc
78601 ccatctctgt ttttattat ttatttattt atcgttagag acagagtctc actctgtcac
78661 ccaggctgga gtacagtggt gcagttatag ctcactgcag cctcaaactc ctgggctcaa
78721 tcgatcctcc cgcctcagcc tcctgagcag ctagaagtgc aggcacatgc caccacacca
78781 agacaatttt tctatttttc atagagatga ggtctcctca tgttcccag gctggtcttg
78841 aactcctggc cttaaatgat cctcctgcct cagcctccca aagtgctggg attataggtg
78901 tgagccacta cacccaggcc ctgtttttaa cttgcaatac cttttctgca agattgaatt
78961 tatattagat tataaagttt gtggacaaaa tagaacactc cattataaaa gcctccttca
79021 tttgttttgt tctctggtgt ttgatttgac tgatgtggat ttgagtatgg aagtgttcca
79081 tgccttatta aggaaagcac tttgggaatt ggccagggcc cacttaactt agtttcagaa
79141 tggcagcact ttggcagtcc tcagtttctc ttatttccta acccatccct actcattaag
79201 acggggctat tgcattccat tttcagggaa tgctctttca tttttcgttg gtgagagaac
79261 atgaatgcct cttaaaatgg tggtttgagc ttgctgagaa tttaggggga tccacagagt
79321 tgaaaagtct tacaggctat cagtgaagca tggagggttt tcgttatgaa aatgtcctga
79381 gatgggggga agactggaca gatgaggtag gggagcctcc ttgcaaagtt agaattcagc
79441 tgtttatact ggtaacagaa tctgcttag taaggatgaa gcaaaaagaa aaacgatatt
79501 aacaccttga gaaaatctct gtattgtgag cttaatccaa caactccaac gatgttagct
79561 acttttcaa aatacatctt agccctttgtt acaataacat ttacttgtgg agtgaaattt
79621 tgtattaggc agattcactg taatcagtaa tcttccttcc attgagattc ttcctgttac
79681 tttcttattt aaaaaccttc agtagcctgc atcctcaggg ttctgtttac agagaccctt
79741 aacagtctat tcagccttac ttctgccatt atcctactc taggctgagt gttaaccata
79801 cctacctatg tacatttgca gctgtgccat tttatctgtt tggattctta acccctctc
79861 ttgcccaagt gcctagtggc gccctgttgg cacgttgagg ggtagcttaa gtgtttactt
79921 ctttccgcac tccctcagtc cgtgttagca gtaccctctt ccatactctt ctattatctt
79981 ctgcatactt ctgtactcca cctatctgtt gccatgaaac aggtcacccc aaaacagtgg
80041 cctagaacaa tactatggac tgcgtttgtg tcccccacc ccaactcata tgttgaaatc
80101 ctggcccca gggcgatggt attaggagat ggggcctttg ggaggtgatt aggtcgtgag
80161 ggtggagccc acatgaatgg gatgtcttta taaaagagac cccagagagc ttctttcctc
80221 ttctaccata tgaggacact gtgagaaaac atctgtgaag cagaaagtgg ggtcctcacc
80281 agacacataa tctgcttgct ccttgagccc ggactccttg agcctggact cctcagcctc
80341 cagaactatg agaaataaat gtgtgggKtt ttttttttt ttttttttg gtcttgtttg
80401 tttgtttgag acagggtctc tctctgttgc ctgggctgga gcaaagtggc atgatctcag
80461 gtaactgcaa cctctgcctc ctgggctcag gtgattcccc cacctcagcc tcccaggtag
80521 ctgggaccac gggcctgtgc caccacgccc agcttatttt tgtatttttt gtagagaggg
80581 gtctccccat gttgcccagg ttagtctcaa actcctggaa tcaagtgatc tgcccacctc
80641 agcctcccaa attgctggga ttacaggcgt gagccaccga acccagccag atgtttgttg
80701 tttaagccac tcagactatg gtatttttgt atctttccatt gtacttaatc tatgggtctt
80761 atattcagca gtattctatg ttatgtaagg agttgtggcg tgaaaccact tcctttcatgt
80821 ttttatgttt ctttttaatt aaatttttaag cctgggaatc ttggtaatga catattatat
80881 gcaaaatatg taatattaga cttgattttc atcagatcag ttttagcact tttcagtgtg
80941 caaaggtggg tggtaatggc tttttccaaa gcatagtccc ttggttgtat tacactatta
81001 atgactatgg gtagtgtcag accccgagcc caagccaagc catcatcatc cctgtgactt
81061 aaacgtatac atccagatgg cctgaagtaa ctgaagatcc acaagagaag taaaaatagc

81121 cttaactgat gacattccac cattgtgatt tgtttctgcc ccacccctaac tgatcaatgt
81181 actttgtaat ctcccccacc cttaagaagg tactttgtaa ttctcctcac ccttgagaat
81241 gtacttttgtg agatccactc ctgcccgcaa aacattgctc ttaactttac cgcctatccc
81301 aaaacctata agaactaatg ataatccacc acccttgct gactctcttt tcggactcag
81361 cccacctgca cccaggtgaa ataaacagcc atgttgctca cacaaagcct gtttggtggt
81421 ctcctcacat ggacgtgcat gaaaggtagc ataatacaat ttttgctgaa gttttgttgc
81481 tcttctactt ttaaattaag gaccagatag gaaaggacat atggtaatct atcaaatata
81541 tagccattga tattttcttt gttttctttc actaaccggt tatgcaaga ttttttaaa
81601 aaaacagcaa aatgaaaagg ttcgtaatat cctgacttcc tgttttatta taaatgagat
81661 gaacaccagg tagtgttaat ttcctttaat ttctttatga gtcatcctca aattaatgtt
81721 tgaggaatgg ttgggtgttt tcaaatatct ccgacatctt ttagttagac agcatagtga
81781 aatggaaaga aattttgaat ctgctagact caagtttgca ttttggctct gtcatttact
81841 catagatgta ctacttggag taatcatact gattttgtag accaattgga aagatаattg
81901 accagtgttt tagggtatat gtatatacac aaaatttgac agacatgtaa tcacacaatg
81961 cttaagcccc atatgttatt aagcccacac tttggtaaat aacatttggg gcttaagcat
82021 ctgtgtgatt ctatatatgc cggtatttgt aaatgtaaaa gtgataccag ctaaatcacc
82081 catcttтctg ggaactaagt acaaaggaat ggtttctgtt ctaacccttt ggcttagagt
82141 atcatagagt tttaaatttg gccagatttt aatttgacag ataaaaaaat gaggcacaga
82201 taaaaaaatc gagaagttga atgaattatg aaaactcact agaggcagag ttgaggacgt
82261 tgtccagtgc tctgttgtat cattatgtca ctgcctgccc tactgttttc ctgctctttc
82321 cctcttcttc ttcctccctc tcagccctgg tccacctacc ttagtgcatg cacacacgta
82381 tggcaaagat caacaaggat gctgggttca gggtcctttt cccactggag tctggcaaca
82441 ctgttcctgc cttgatatgg ttcttggttg ttggYcactt aaaacaatgg catatttgа
82501 agggctgaat agacttcctt ctttttaagc ttttctttt atttatactt tttggatccg
82561 tgtaatttct ctgagtcatc cacattattt tctacttttt ctcagttttc atgacctgta
82621 ttaccattac aggtgtctct gctataattc aatatacata ttcctgaaaa cctcatgttc
82681 tacaaaatca tacattcaga ataatctggc taatgggaaa tattggtttg gggcagtctg
82741 gcttatggga aatattggtt tggggcagtc tggcttatgg gaaatattaa gttgggacca
82801 accactctaa atctatgcta ctttgcaagc acagcactaa caaaaacaat gaaaaccatc
82861 ataaaacagg agcacagttc agaagacata ctacattcct agaactttgg gatacacttt
82921 ggtaaatatg actttaactc atgaaaatat gcggggctgc ttgatggaag gggatgtaag
82981 gaaggatatg aggctggtga gtactgggag acaagaatga aacacaccaa gacgtttgca
83041 tgagatcatg caaagagaat catgcagaag gtacatctaa gacacaaggc caaccgggca
83101 tggtggctca tgcctgtaat cccagcactt tgggaggctg aggtgggcag gtcacaaggt
83161 caggagttcg agacctgacc tttaacagtc tattcagcct ggcaactatg gtgaaatccc
83221 gtctctcacta aaagtacaaa aaattagctg ggcgtggtgg cacgcacctg tagtcccagc
83281 tactcaggag gctgaggcag gagaatcact tgaacttggg aggcagaggt tgcagtgagc
83341 cgagatcaca ccactgcaat ccagcctggg cgacagagcg attctctgtc tcaggggaaga
83401 aaaaaaaaaa aaaaacacaa ggcccggcag gctgagacca tgacaggaac ggttagagtg
83461 gaccctggtg cagtgtgggg tgctctgttc agcctcacta tgaatttcac atccagcttc
83521 tgttacttgg agatataaaa cagtaatgtg tggagacaaa tcgtggatga accaactcct
83581 gagttatggc gtcatcaatc tgctatgacc agtcaaattc gcagtataga aacatgtctt
83641 gtagctggac agaaaacatc cagctctact gctgctaaac atcatggaat gtacccattg
83701 gtttatccat atagtaagtt ttaacattat ttttaatata ttgttcattc tgaatttgac
83761 agtggtctgc caagtctccc tgaactccac aaattaaata aaggtatctc agagggcctt
83821 tcccaagaac tttaatgcca tcttcctagc aagctataga aaacatttga aaaccccaag
83881 ggcaaagttc cagggctgcc tagggggcaa atcagtgaac agagtagtaa actgataaaa
83941 ccagcataga ggcctctgtg gggaaaaag acacctttct gcagttaata aaatagtacca
84001 aagaacactg attgtcttct cagggtttgt agcccatttc tgttttttat ttttaaatct
84061 cacctgttat ttttgttttt agctgttcca tagtagtctg atggaaatac actttatgtg
84121 ttcttgtgtg ccaatcaaaa ataaaataag cacaatgaat acctctaatt gcatagttca
84181 tgaaaggctt gaaaagatgc agagcagctg gctaatgctg ccaatgagcc attggctgga
84241 gccccttgta actcagcctt tgattctgtc ttcagcaagc cccagcatcc tcagggccca
84301 tgtgatgggt gctcagtgga actccagact ttgtggaggg ctctgtggtt ctgctgctgg
84361 ggaaactgtg tgtttctgag cctatgggaa tgggtcagaa agcctgggaa atggggagga
84421 ataggagcag gaacacaaat gaggagccag caatgcaggt tgctattatg tcgcatgtca
84481 ctcctacgca atatcttgat agattagctt ccttcaggcc caaaaccttg aatggacatg
84541 aaccacagta tcagggctaa atgagtaaca gcccaaacca ggtccactct ccagacagtt
84601 agaaaaggta gacatctctt gtagctggat ggagcaggag tctccccag gggtggtaat
84661 tcagcaggtc tttaaagaat gaatagggatt aaagtaagtg aaaatggaaa gctgaagga
84721 gggaaggaaa gtgaggctca gggagaattc tgggcaaggg aaagttacag agtgattcct
84781 tagagcttgt gagtctaaca attttgatgt caatggacct tattcttgga accacagggc
84841 aactgattga ctttagtttt ctttttttgct atattcttgc catctcactca atgactgctc
84901 attgaaaatt gatgataatg gccatatgga aagtctcaga gcttatctag gatttgagtc

84961 cctgaggcat aatcagtggg tggaacagca gatggatggg gcagactatt tttctgttcc
85021 ttcctgtgac agttgattat aagtatataa aatgggcatt ctctttgtga tcttagcttc
85081 caaaattacg gaaggttatc actatttatt attactactt tctcagcaaa ctcaaagaat
85141 cagagtgata ttgattattt agatttagca atgggggact taagctctta taaatcaggg
85201 tcatctgaat ctaaagatgt atgtctttct tatttcagtc tgaccagtta tttaagaatc
85261 caagatacct ttacttttta tttgaagttc cttaatttga tagagctctt accaagcagt
85321 tggttctgtt tctctttcag ttctctgcca agcttttgtg tgtcttaaga cactgggact
85381 gggaaagaac tgcagtgttt gttaaatgta aattatactg agccttgaag atttgaatgc
85441 atggggagag gtacattttg gctttccttc ctttgtaaaa tgcagttaaa ctgatatcca
85501 gaacaatggt gagaaaacac caattaactg aatgtatgaa agaacagtaa ataaacaagg
85561 tgggcagtcc tgtatgtgag gcatttttaa actctttgct gtgtaagtgc aggcttttgg
85621 aaagatctgc ttttcacttt gatttttgca gtcccacacc agcttgcttc tggttctgcc
85681 ttcagggaca tatgtgctct ctagatctgg gaatcttttt gtctggagac ctcaagattg
85741 ggatctgcac cctcccacc ccttcctgtc tgaactctat tttagatctg cagtaaagac
85801 ttgaggcttt tgtcaagctt tcaactctga ggtatttttgg aaaactgtaa tttgtttgt
85861 tctctgctgt atgcatgtgg tttcttaaaa cacgagtgtg attatttttct gcatcctttc
85921 catagcaaac atttccctca aactacatgc tccaaaagta ggttctcact gcacttgcca
85981 tgccgtctca ttgcttattg agagtgactg tctctttaca acaaatcaac tggttacaat
86041 tttgaggctt tttaggtggc ttccaaactt gtcttggggt ttgtccctca tatgttcagc
86101 agccaaacat gctcaatgca ttgtatattt cccagcaagc catgaagcac tattgactta
86161 ttatgaaact taatttgatg ataatgaggc aggtctataa aatagcactt tgggtagttt
86221 ttacccataa aatagcaatt tgtggaagac cgttagtatg tagcatggac tctgaagcta
86281 gagaacttga gtttgagtct cagcttttct acttttttt tctagtaatt ttatttattt
86341 tatgttttac tgttaaattc ttaacctacc tggaatttag tttggtatag ggagtcatgt
86401 ttggatctag ctgttgattc ttttaaata taatttttag tgatttcttt attgtgataa
86461 aatatacata agatttatca ttttaaccat tttaatttag atgtacattt cagtggcact
86521 aaacacaatc acaagttttc cacttttag ctgtgttaga ggtcaaatta ttttaccttt
86581 ctgcgtctcc gtttcctctt ctgcaagtgg gaataatact cccattaagt tgttatgaga
86641 ttaagactta attcaggccg ggcgtggtgg ctcacacttg taattccagc actttgggag
86701 gccaaagcag gtggatcact tgaggtcagg agttcgagac cagcctggcc aacatggtgg
86761 aaccccatct ctactaaaaa tacaaaaaat taactccgta tagtggtgca tgcctgtagt
86821 cccagctact caggaggctg aggcagcaga attgtttgaa cctgggaggt agagtttgca
86881 gtgagctaag attgtgccac tgcactccag cctgggtgac caagcaagac tctgtctaaa
86941 aaaaaaaaac aaacctaaat tcataggaaa cttgatgtga cttgatgtgt acaggacaaa
87001 atcaagtgctt aataatagtt gatggccatg aggatttgtg gtactggcag tcccccattt
87061 gctagttaag aagcatttt tgagcctggt gccatatgtc tgcccatac atatgcctgt
87121 gtggtcacag taattgccgg ttgaatcaca gtggagacct cgaggattct cattggtaac
87181 actggataat ttttcatca tttttatgtc cactttagca tgagactaat atacagtttg
87241 aacttcaggg gagaaaagaa gattttctaa cagatttata ttttcaaattg tttacaagac
87301 aattgaaaat gaaaagataa aacctactta ctcttcaagt tcaaggcata atgcaagagg
87361 cttgaagagg gtagacttct gaatatattc catcaaacagt atctctttc agaggttttg
87421 agaaaccct tgtttaaaaa aaatatgagc aacaattatt tgttattcat gaattctaga
87481 tgtgtaaatt gtgtgatcaa aatgagagga aaaagagaag tctcaagaga atcagcattt
87541 tgtctacatt taagtctttt ggaaatgata tgtttgaaaa taatataccc gttaaatata
87601 tttccttaaa ttatttagat aaactgtttc tattgtagtt tctggtaaac agtaatatga
87661 aatggtttct attttattgt caacaacttc attactttt aatgcagcaa aaagcttcca
87721 aatagatctg ttaaaaagac tgcagaaatc ctctgaattg aataactat ttctagcctt
87781 aacatctcatg cttccacagt ggaatatact atattcagcc accatcacaa aaaatgtctt
87841 tcttatcagt gctgccctag ctaaatgtga actttaaaaa ttggaaaatc aggcactttg
87901 tagacagttc actctttgtt tcatattttt gggctaagga aaaaaaattg cccaaggaag
87961 tatttctgga aggagtctaa cttctcaata aacatagtag tttagcctac aatatttttg
88021 ttgttttggg aattgatagt gaccctaaat atatacaaag aatattgatt tctaaagcat
88081 ggatcgtgtt ggttcctaaa aagtgagtga taatgtagca attaaattct gccctgtatt
88141 atacacagtt ggtcagggta tcagcagaat gccatcatca ttatgaatt gtgtaataaa
88201 tacttggggc agagtgccat agtggaaata aaactacatt ttggtttagg acttcctgcc
88261 ctagcccatg gcctatagag ccaagccttc acgtttcaag aagttgtgag gggaaagaga
88321 caggcattgg cctcatggta gcagctgctg gagggttctt ttcctagctc attttctttc
88381 ctcatgtttc acatttttcc agggtgacat cacgtgtggt aactatttgt atggatcttc
88441 caagccccgca ttttagccaa gacatttctc atgggctcca gacccacaat ctggtggtca
88501 acatactctc tacttggttg ctccatagat accctaagtc aaggcatgaa tatctaaact
88561 gatcgtgact ctcctctctc ccaccatcac caaaacct gtttctttc ctgcatttctt
88621 ttttttttt ttttgagatg gagtctcgct ctgtcgcccg gctggagttc agtggcacga
88681 tctcagttca ctgcaacctc catctcccgg gttcaagcga ttctcctgcc tcagcctcct
88741 gagtagctgg gattacaggt gtgcaccacc atgccccggct aatttttgta tttttagtag

88801 agacggggtt tcaccatgtt gttcaggctg gtctcgaact cctgacctcg tgatctgccc
88861 gcctcagcct cccaaagtgc tgggattaca ggcgtgagcc accgcgccca gcctttcctg
88921 catttctttt gagcatctag cacgtttcca gtcattcatc cacgtcagaa agccccagat
88981 gccaccagct cttctttgct ttcaatgttt aatggaacac taaggtctgc gaattctacc
89041 tcacaaatgt cttccctggc gaatcctcct ttctgtgcca cccatcttca ccttatttcg
89101 ggccttcctc atttctcacc tggatctttg taaccatggc ctctagagct ggctccctgg
89161 atccctactg gccatcaatc ccatgtgcct cagccgtaat gccagtcaca gttctcaaag
89221 agctattctc ttcctccctt cctcattcag gctgtgcctg gtaatctgga gtgaattttc
89281 cactccatcc tgcagacttc caaatactta tccagaggct cagcttacag ctcaatgcct
89341 ctttgaagcc tttctcaacc tttgcagagt tgagatataa ctatgctgct aaatgtaaat
89401 ctaactcttc atacattttc tcttgtttac ctgtctcccc ctcctgtcag agtctgagtt
89461 acttgaggtt gtgaattgag tcttatttat gtctgtctct aatatctagc atggtgtgtc
89521 tcattgatag cagacatcta taaatgagtg agtaagtgag ccaacgtgtg ggtggttttt
89581 cctggggcgg gaagggttgg gagggtacca cgtagtcagt gtgagcctcc cttcgggctc
89641 tttgactttc cgatgagcat gcttactggt agtgacttcc cttgaccctt accagttaga
89701 tacatgctct gggaccagag ctgcagaata taaaccagta gttttgaaaa gttattatta
89761 tctccataag gattgggttt tttataggca caggtaacaa ggttgaacac aaccaagtga
89821 acccagtgaa ttctatttat ttcagtgagg tgtctgtatg cactgtggcc atcccagagg
89881 ccttactttc aattcatatc cactaactca agggggcttt actgccaccc agcactcaca
89941 ccgccgtgct cttctgcaga gactttcccg cagtctgttc actgcttcat actttctcct
90001 gcacttaaac ctttagcata tctccatccc tgcctctcag ctaacggggc ttgcaggcaa
90061 ttagaaagag cttccctgtg tacctgccac cacatcttct cagttgtctg cactcgctgg
90121 ctagtctccc ttgctgtgga ggaattgttg atgcccctgg gaaggccaca ccctccactt
90181 gaaagatccg gtcccctccc accttttttt ttttttttt ttttgagacg gagtctcgct
90241 ctggtgccca ggccagagtg cagtggcacg atctcagctc actgcaagct ctgcctccca
90301 ggttctcacc attctcctgc ctcagcctcc cgagtagctg ggactacaag tacccgccac
90361 cacgcccagc taattgtttt gtatttttag tagagacggg gtttcagcat gttagccagg
90421 atggtctcga tctcctgacc tcgtgatcca cctgcctcgg cctcccaaag tgctgggatt
90481 acaggcgtga gccaccgcac ccggcccccct cccacctttt taagaacatc actccatcag
90541 ttgtctcctt tctcttctga ataatcagtt ttcccctggc caccaagcta ttcccatcag
90601 catacaaaca tgctgatttc ttcccccata ccatgcccct ctccagcttc catttatctg
90661 ctctgtttta ctttgacttg cctgaactca ttataactta ttcctctcct ttcagtctct
90721 ctctttgcaa agtttttaaa gcttttaatt ttggtaagac atatacaaca caacatccaa
90781 cttaccatgt caaccttttt tttttttttt tttttttttt tttgagatga agtctcgctc
90841 tgtcacccag cctggagtgc aatggcacga tctcggctca ctgtaacctc tgcttcctgg
90901 gttcaagcga ttctcctacc tctgcctccc gagtagctgg aattacaggc atgtgccaca
90961 tgcctggcta atattttttt gtatttttgt agagatgggg tttcaccatg ttggccaggc
91021 tggtcttgaa ctcctgacct caagtgatcc acctgccttg gtctcccaaa gtgccaggat
91081 tacaggcatg agccactgcg cctggcccat ctcaaccatt cttaagtgtg caattcggta
91141 atgtcaggta catttacatt attaagccac caatctgcag aatgttttca tcttgcaaaa
91201 ctgaaattct gtacccagta aacattaaca cctcattttt ccctcctcca agcccctggc
91261 aaccatcctt ataccttcta tctctgtaaa tttgactact ctgggtaatc gtccattctc
91321 tcctgaaccc accttcatca ggcttttgct cctacattcc ccctccacca cttttctcag
91381 ggtcacctgt ggcctccact tgctggatct gacagtcatt tctcagtctt tggctgattt
91441 ggcccggcag cagctatagg aacagtggag cactccctcc tctttgaaac actgtcttca
91501 cttggtttcc agggaccttg ctggcctgtg ttttccttct tcctcacaga ccactcccctt
91561 ttagtgttct tcctcttgtt gcctctgtag gttggaatgt cccagggctg agtgcatggc
91621 cctcttctct aatcttcact cactcctctt tagagttgat gtctttccat gccatttata
91681 ctcttacagt tcccaacatt tgtcccgagg cccagctgtg aacacttcct tacctgcata
91741 tctaataggt gtctcaacat ttgcatctcc agaatgactc ttgacctgcc ccccaatatc
91801 tgccataggc ttccacatct gaggatggca actccgttct tccaatttct gaggccaaaa
91861 ttgggaatca taattgacta ctctttttct ctcaaacccc catccaatca gcaaattcag
91921 ttggctttac tttcaaaaga tacaacctga atgtgaccac ttcttgtcac ttccactctg
91981 ccactcaggt ctaaccacca tcttacattg cttgggttgt cacctcctcc ctggcctccc
92041 tgcctgccct agattccaaa cacaaatcta gcgagaagag cctatgaaaa tgtgagccac
92101 cctctgctcc aagccctcca gtggccagga aatggcagac ttttacagtg gccgaaagct
92161 ctatgtgatt gcctactcca tgacctcatt ggcctctttt cttgatttc tcacccttgt
92221 cccctcgctg gagtcccaca gccttccctg gtgtgcctgc agtatgccat cctgctgcta
92281 ccttagggct tttctgctct ctgtccctct ggggaaaggc tcagccctta aggatcccgt
92341 gccttcctct cttctttctg tcagctctgc actcagctgt caccttggtt gcgaattctt
92401 ccctggtcac cctgtttaaa gttgccacgc ttctcccgca cttcgtagtt ttttttttct
92461 tMttattttt ctttctagcR cttaccaccc tgtaacatgc cgtatatttt acttgtcatt
92521 tgtgtttgta tcaccccact ggagggtgag ttctagagag cgggatttcc ttgccagcgt
92581 tcgctggatt tgcccactgc ttagaactat ttctggcgca tagtaggtac acagcaagta

92641 ttccttgaat gactatagag aagaagcttt cacaaaacag aaaagcgtaa ttaattgccc
92701 acttcagcct cctaaactgt aggcttcatt tgaaatttca agttcttatt ttatccaaaa
92761 gagaacaaag ctgaattaaa cattgcttca aacgatatct ttgagtcgtt tccaagaagg
92821 atgtatagat gaaattataa tttaggttgc tatggataca tttatacata taaaatattt
92881 gtgacaaata tagtatttgt attatataca agaaaattac tatggatttg caaatcgatt
92941 catataaaat ttacttttctt atgggacatt aaatatatta cagtagcttt gaatttttctg
93001 aattatattt acttaaaaat gtcactggca ataccttttga ggcttttctt ttttggataa
93061 aacttgtggc aataattcct cctttgactt cttcagcaat atgttaaaac tggcacggaa
93121 cctttgaata gcttttgaat ttttatctcg tttgaaatta accagttact gatgtaatta
93181 atacccatatg gtataaaattt tgaattctgc atgatttcta cttcaaaatg atgcctgctg
93241 ccttcattct acttttatgtt taacacaagt atttggaaaa cctgagtagt ggttatctgg
93301 cttagtggaa ctataattta ctgcaggtaa aaaggaggat tcatttctttt atgttggaag
93361 tctttaaaaa tatactgata catttccatc ccaaattagc aagtctgtta gagggacaat
93421 aattttatct ttgctaactg aagatcctac atggcctcat gcctaagatt atttactaca
93481 catlgtatca aaataaaaaa agtttgatat gccactaaaa ggctttttta aataggagag
93541 atctaatcaa tcacatacgt ggacgtgctg tttatactac aaaacctcta gatcctcttt
93601 acctttgcaa ggggggtggg tagttttggc tttccttatg tttttatttg ttatttgtga
93661 agtatataat aaaagaaaat ctaagaaatt gaggattatg gttaactgaa gtgtaatcga
93721 ctgtttcacg gtatatttga cttcaacagc ttccagcaaa gaaaaatcct ggaaaaaaac
93781 tttctggttt ggtcattttt attataaaag gctttctatt ttccagcaaa gaacatttct
93841 tttatggtta agagtttcaa tatttatgta attagcaact cacagcagtg ccttgtttca
93901 ttcttgattc taatcctgga agtataacat accagcaaag cagcagccgt agcgtccaca
93961 gagcctactt ctctgccttt tttctgtctc cctgtagaga gaagtccact cttttctctg
94021 atcccagtgt agtaatgtaa atttgggcat gcagaaagtc aatgtgcctt agcatccttg
94081 ggattcattt tctttgcatt tccgaaatta ctcaccttgt agcagttgtc agatccctta
94141 attagtaact agttttcttt gaattatggt atcacatagg ctgtctgtgg tctggctggt
94201 aagagactgt taccagctgc tcagctttag tcaggcaata aggtatttgt tacactccaa
94261 ataatcatgt gatttagtga aaggccattt gagctctaaa gcctcacagt ggaaagttcc
94321 tgagacctct gccctccctc tcacacccca gagaatccct agtctcctgc cttcctctca
94381 tgctatctgc atgattgctg ttggcctgct cggccaggaa gatggtccga cacacacccc
94441 tgttcactgc ccagggtctc aggatccctg tcctaggcag agtcccaagc agtgttgtac
94501 ctgccaggaa gccctttggg ctcttctgca cccttggggа ccagtgtccc tacagtaatc
94561 gtactcatg tttattccca tacttctctc tagaatttaa gtcatgagct gtgtgtctcc
94621 ctttctgcac tcagagagta tcagaggagg cctggtgtcc tagttatatt tcatttttca
94681 actgtcattt gttgaactcc agacactgct aactgctttg catgcatcat cttacttctt
94741 cttcccagtg tttataaggt gcaactgaac caagccatat agttggcact gtgatgagtg
94801 agggaacaga tacattgatc attgaatgga gctagagaaa actgttaagt aagttgacta
94861 ctaatttagt ggaaagagaa accttcaaac taacttacag attgttcact tattgtacaa
94921 aactattatt tatttatttg tgtctcatgg aacccagtaa tagctaacat aatcatgata
94981 gcagttattc ttagagtgct tcactctgtg gcaggcactg ctctaagggc tttatatgta
95041 tcatcccatt cagtcctttc actaattcaa tggagccagt actattaatg tcctcatgtt
95101 acagatgcag aaattgaggc atagagaaat taagtaatta cttccaagtt catgcagcta
95161 agtggtggga ccagagtttg aactcaagct gtctgacatg aggacctgga accagcctgg
95221 gtttccagca agataggaca gtgcccatct tgggctgggt ggaaacatgg cactgaagac
95281 atgggctctt tgttctggag aaaatattag ggacctggtc agagctcact tacttttagt
95341 aataaatatt caattcaacg aatatttatt aagctcttac tgtacaacaa tgaacaaagc
95401 tcctaatctt catggagctt acgtctagg aagggaagag agaaaattca catctatcta
95461 catgactaaa tcgcattgct atgttagaag gttatttatg tgctaagata aaaagaaaat
95521 gtagaacaga ggaagaaggt taagatggtt atgaaagaag tttaaggag atgatcaggg
95581 aagacctcat ggttcatatt ggagaattgt tgatcacatt tctgttgtgtt gacctgactt
95641 ctttgttgat ctcttaagag atgcaggctg agatcttgac tcactcaaca cttgtaggga
95701 actgcttaat atttctgcct atttaaccct ggaagcgttg ggttgtttgg tctgcagagt
95761 caggggtgag tcagcccatg ggttctgctt tattggctgg gtagcactcc cttactggRg
95821 ggcagttctg aatgtgtgcc ccatgggtgc tgagttatgg gctgggtggg gtgtctagag
95881 gagtggggag tgagggtcag acaccgagga cattgcggag ctgagagagg aagttcagga
95941 tggatagaaa gatgtagctg cgattcttct agagagaccc ttgcctgcct aggtgaagat
96001 agggatgaat tgtccaaaga gggcacatga ccctagatcc tacctctacc caaggactat
96061 cttcaccaag gcagtggtcc caggaagagt agcaagaggg tggagataac agagcagccc
96121 cctcagtact gggaaaacag caggttccat gcacttttgt ggtgggccag ggcttagat
96181 gagtgaatga cagatttacc ttttacccag ttattgagac atcatgagga gtgttaagat
96241 tctgaaagta aatttccacg ataacatgtt tatgRtgtca tttggtcttc ctctgtggaa
96301 ctggtaatga ttttgacttt caagatgaga tcttctcttc tgaccataaa acaagatgtt

```
96361   gcaaacgagg ttcccagctg tcctggtctg tcggcatggc tgctcgatgg ctctggtggc
96421   tgataactca ggatgttgtt gctggagagt ggggaactcg tccagatcct cctgagacac
96481   cactttcctt tttcatacaa
```

ERG genomic sequence (SEQ ID NO: 4)

```
>21:38703451-38882000

1       tgacagattc taaagtgttg tttcaacagt ttcttcttcc tcaaaggtga gcatcatgtg
61      cacactgtca aaattaaaaa aaaaaaaaaa aagacccaat aaaacccgat gaaacccaaa
121     gagcatggag atgagaaact cactgctggc tgacgatctg aatgaatggc cttgggggga
181     atgtgaatgt ggaggtagca gaagggtcct gtcttcagtg cttgattctg Watcaatact
241     tggtaaattt aaaaaacaaa aaaaccagca agggagattt taaatcatca aggcagaagg
301     atttaaaaag tggaatgtgt taaatgcaag agtgcgggat ctttgcataa agttattata
361     ttttcaaaaa ttcgacaagc attgttttta ccaaacgtgt ttaaagtaac agccctgagg
421     ttaatgttat gattggattc tgatgtggca ctttaaaaat aaatcatttt gcttggcctt
481     agcatttctt ttcaaaatgt ctctgtactt atctgtgtac aacagcagat taccgttctt
541     cccagagttt aattccatga acaccctgct gaaagacttg ttaaggcctt atggaaaact
601     ctgacctgcg tgttcattat tgacgcccaa gacgagtgca aggaagttga tacttgggat
661     gaggaaattt aaatcagcag ctgatctgga atctggaagc actgcccctt ggatctcgcc
721     aaatatggaa agaattcttg tcactgagca aatatagaat tcagtgctag agttttacct
781     cttgaatttt ctagaacttt gttttgatta gccacctaga gtataagaat tgctgcctat
841     gggatttttc ccagaagagt agataacata aagtaaccag cRataataat tttcattatc
901     caattatttc atgtgtctcc ataacactta atacatcatg tttctctgca cagtaattcM
961     ctatgtacag ctagggtgaa tagcaggaaa aaagagatca gatgataaag agaagggaga
1021    cagatttgtg tgacttgtat aagatacttc gcctctctaa tcctttgtcc ttatctgtaa
1081    gaaagcagca gtacccaggc tgctgtgagg atcacatgag acattatgag agtttagcac
1141    aggacttggc acataacaag cagttattag gatgatgtta gtttggatta tgaMttcaag
1201    atactacagc tacatttttt atactttctt aaacatcaat ttaagtcaat tttaattaac
1261    gttatttcac taggagaaat gtctctaaaa acataagaat tctatttgaa gtctacaatg
1321    ataattacat tactctgata tcttaacttc ctctttatga tttcaaataa ttaaaattta
1381    agtttatgtt ttcaacaagt gcttattgaa cctctactct tgtccagtca ctgttgagga
1441    cacagaagaa atggatаaga tatcactaaa aacagctttct gcgatatcag tgggtataca
1501    taaattattc acactcaaca acaaacacaR gcaaagctgg gagaatgtgc tgacaggaaa
1561    gaaaatgaag agtgggagag tggacagatg ggaatcgatg tgaaatttta taaaacatgt
1621    cttggccaag ctcagtaggg gaaatatgtg gaaagtaagc tagaccaaac agRgaataaa
1681    agtataaata agaaaaaaaa tccagaggtc acagtggacc actagccaaa atgggttcac
1741    agcaaacaaa caaaaaaatg taatgaaata ctaaaattaa agaagtacaa ataaaaatga
1801    gattctgttc ttatctgtca gaatggcaaa gattcaaaga gtaaaatatt cagagttgtt
1861    atgggtgtag tgtggaactg gtctcatatg tggctagaaa aagggagaac tgtgtataatc
1921    cttcagaga ataatctggt aatatttttt taaattggca aatatttaaa tttggcaaag
1981    acttaaaaaa tatatatacc cattggctca ataattcctt tctaggcacc aatactaata
2041    aaaagtattc aaaaaattaa atagatggtg tactgcaata taatgagtga aacatYgcaa
2101    gcagcatcac tttatacact aggatattgg ttataaaatg gtaatacata ttttagatag
2161    aatataatga aacaaaaatt ttgcttatca aaaaatgtta gtaacatggg aaaatgcttg
2221    taaaacaatg ctaactgaga agagcaggac aggtaggtag atacaaggcc aaacagatac
2281    acacRgtgga gagacatatc ccaattgtta ggaatttgct gtggttggtt aggatctgaa
2341    caatttatat tgactttgtg atgacttttа aacgttttct ctaccataag aatttttttat
2401    gtttataatt tatgctaaag aacaagatgt atttttgta attcaggagt aaagaggaga
2461    gtggggtatt ccagggtgct gttcctgccc taaccaggag cacgatgcag tcatagggct
2521    ctgccctcct ccagcagcct cggctcagaa caggacgaag ccaacccctct ctgaccagca
2581    ccacctcggg cgacccctgg acgctccacc tgccccctgg tgtggtaccт gccctgctac
2641    acctttaaca agcacccctg caagctccct cctcttcct tccctgtcct gtggctgccc
2701    agcccgagt gtaccctgcc tgggtgtggg agccgccaca tcagagcagt ctatggctgt
2761    gggcttcaca gctgaagctg ggccgtggga aatgttgaga cgagtgagtg cagagcctga
2821    aagacaatac ggtagaaaag gttacatccg cgggggggcg tctgatggca tctgccattt
2881    attgaggatg ggtgcgagac agggtagcca ttatgatccc attttacagg tgacgaaact
2941    gagatcagac aggctagcta ccttgcccag ggtcacaaca ggaaggaagc aaatgcaagt
3001    gtgtctgcgg ccacgtaagg tgagagaagc gctatcaggg gtggtctgac agaatcccca
3061    ggccagggag cagttgtcct ctatcctgtg gggtcaaagg aggggacaag aaggctctcc
3121    ttgaggtagc tccaaagaaa agaccccgcc agagcacagt gtgctaccaa acgctggaac
```

```
3181 agcctggaga ctgtccctgt ctcttctctg aggtttctca tttcagagaa actctcatcc
3241 gtctggcttc cccatggccc ttactctgtg attctcttat gtatcagctg ttaaaccaat
3301 aaatccgcca aattgttggg atgcctataa tggctttggg tctccactcc cacagaggga
3361 atcttattct aaagttctaa atgtatcagt catattttcc tgaagacaac agaaatggtt
3421 gtttcattta cttattttta tgtatgcttt ttcaagagtt gttaacctgt gtttgtgttt
3481 aaataaagat ctgttttgca aaacaaaaac tttatgagat aatcacttat aaacgtagat
3541 aattaagaaa tggttcaggc tcagcacatt gtctgagagc attgcagtcc tgcactgtat
3601 ttcatggggg aagaaaagcc cacagatgga gccattctca atcctgcttt ccagggtcac
3661 tgagtcaggg tgcctggcat gcatgggtgc atgcacacac aggcagaggg ccagggagaa
3721 ctgtgctgtg tccacagagg gcagcctgga tcacagagct gaccaagaac ggaagcagca
3781 agttgtttta aagtagttgc ctgtaaagcc acttttcggc aaggacaaac actcagagca
3841 tgctctgaaa tgacttatgc acagcagggc agcggcattt tgcccctggc cttccttcca
3901 ttctcccgga atccccctaa agtaacaagg actgacgcaa ttcgtatttc acttagccaa
3961 caggttgatg aaaaatcata aatctgtagc tattaaactc attaatcaca tccatcaaaa
4021 ttctgtgagg agttaacttt cttcatataa ctcttagtct taattaagtt tccctcacat
4081 gtgatagcaa acgttcaaga agtgcaaatg tgcagacgtg gcgtatataa tgcaagcttt
4141 atgtctttaa attaataaaa ttgagtccta tcaggtcgtg tttcaattac catcaaacct
4201 tccaacctct gttaattcaa aaaaaagtaa cttctttagg caagtcatgg aaatagcact
4261 agggtgccct caggtctcca ccaagccttg ttagtaactt tccatgtcct gtctgatttt
4321 taagatgctt tcccctgatg ctgctgccgg ctgctggctc tctccacatc cttcaatgtc
4381 agatctctgt gatgatggaa aatcccccac attccctttt tacacattaa gtatctttct
4441 aggatcagaa cttgcaacct ggggttcatg ttctccttaa aaggtccggg gagaggactg
4501 tatttctgtt gtaattctat gtatttcttt ttaggcacca gaaagtatta ttctgagaaa
4561 ggactgtagg cttcactaga cttcccaaat tgcagatggc attaaaaaaa aaggaatcag
4621 gaaagtcttt gggaaattag gctaaaactc ctaactgaag cacaatcgag ttttcagtgc
4681 aacagcagga tccctgcagt ctgtagcaaa cactgagatg tttgtgggga cagtggggcc
4741 ggtgaggttc agcacctctc aatattgtca gatgtcacca atgcccaagg gaagcaccaa
4801 aaccaatcag tgaattgtct gcaaaccatc agctttgttg cttccaagtc tttactagaa
4861 ctcttaagct gatcttaaaa ttcacagaca cttagagata aatgaacact ctcacataag
4921 ttcccaaaat tcctttactt cttccaattg aaacattttg ttcccaattt caagttacca
4981 agggaaaatg atggtaagaa tcacaaagac tggatacgaa tatttagctt ttcatagtgt
5041 ctcatagggt cttacaaatg ttaatgcaaa aaaataaaaa ctccactcaa atgcagaaaa
5101 ccaacttaaa aaattcagag catctgatac ctaatcgact aattgattta tttactgaaa
5161 caacaaaaaa acagagtgca ttgagactgg aaattgcctc tatgggggc tgtttcctaa
5221 ttccagtgga cagccatcat tttccctatg ctaacttggg ctttgcgcta acgtaattga
5281 aactgtagtc aacagactca ggacctcctt tttccactct ataaacaagg ctgtaaaatc
5341 atctcattac tttacccagg aaatctaaca gaaacatgtc ttaaaggaag tcacctataa
5401 agagggccta ttttaacaga agattaaaaa aaaattcacc tgtagtcatt ctaagggttc
5461 acttgggtac atacaataaa cacataatgc aatgtaataa aatgttaaat caagcatagt
5521 accttagaca agtgtaaact attatttcca aaaaagtgtt cagaaaatca caaaatattc
5581 aaactttcaa aatagcttca tgtattcata aatgtatact tcaaattaaa cagtataaca
5641 catttggatg ttttgcaaaa tgtacctacc ttctaaagga tggtctgtta tttcaatgtc
5701 ctttttaatg cactgagttt tttgggaaaa aaaaccacat aagatcgtac ccaagctatt
5761 caagatttac acagaatatt tgatttaaca tgcatatgaa taaggatgaa aataagaaca
5821 aaaaaataac attttgggtc acaaaatcaa gtaatttcta ttcatgtagc taYaagtagg
5881 gcacattaac tctcaatttt ataattcctg tctataggag ccatatttca gcagattcca
5941 atccttgaag ccaaagaaag aaaagtataa ggtgaaagtt cttggtacac agatttttaa
6001 tatattattg aacacacctt gagaaataaa agctgaactt ctcaaacaca gtttctatgg
6061 tacatatgag tcaaatcttc taatacaaac atttcaaatt atgaaaatac caaaccaaag
6121 agtattttttg aaaatggctt ggcccaattc tgggcaaact tccattttct tatgcacttt
6181 ccaacaaact aaaagcctta tgaaaacacc accaaatgct tctcacctcc gtgcagcaaa
6241 actaaagaca tgcaacaaac acaatttcct tttccctcca ctcagcatct gcttttgttg
6301 ctgatttttc acatttctac aaatgtcacg aaggcatggt ggcctttaaa acaactgaac
6361 ggacccccat tcaagactgc atgcccctttg acttgtagtc accattaaat tggcttcatt
6421 tccaggaatc aggccatatt taggattgta cctgtgcaga tttacctcca cattaatctc
6481 tacatgctat ctactaaaaa cttaggcaag gaaatgcatc agaccaaaca ccccacagca
6541 cagagaaccg accggccatt gctttccaat ctccgcaaac ctaaccattg ctggaagaaa
6601 tcttactcac agtgcacaga cagtaggtat tttattgaag ataaacatat agtggaacaa
6661 accaaattac ccccatttga gttacgtgag cactcagttc tcagcgtgga tgtcccacaa
6721 atcaagtcaa catttgcgtc ccattaccag cagccacttg ccgagtatct cttcgcttcc
6781 actgggactg cctggcatcc ctgatgctaa ggagccactg aagagcctcc aaatgtctga
6841 cattcacaaa cgcatctttt gctttgaccc gacccttcaa cctctccgag tctgctgcct
6901 tttctcagac acacatccag gcaccgttag ggatagttag agaatctgaa aattcagaag
6961 cgctccgaaa agcctttcca aaagtaatcc acagcactca acagtgaatt tagaaacccc
```

```
7021    aatttttttc tgagtttgaa gtttttaagc cttgcggatg gttggagtag gaaaaaggaa
7081    attactagg cagtgcaaag gaaatcttgt tgtcctctat tgtggcagtg ggggtgttgc
7141    ccaaccctaa cttatctgcc ttgataaagg aaaccaaaga aaagagtaac aagaacaaga
7201    ttttgtcaaa ttaaaaggaa ccctttcctt accttaatag tgctggccat aatgcRatca
7261    agtttattga tcgttaataa atgttaataa taattattgc ttctctctga ccagaaagta
7321    gttttgatga ggttgtttag agcggatgag attgtgctaa gtctggaaaa tgaagtcagc
7381    caatggcagg aagaggtttc tattggtcct ggctgtccag cccaaagaaa caggatattt
7441    gggagtggag agataagaga ccctgaaaac aatgttgttt ttcttgatga tatgcagcca
7501    ggagattttt ttttttttaat taaaaaaaga aaaggcatca attgggatgg ggactgccac
7561    agcaggtgtg accggtgtgc cgccgtgtga cacactgcac tagagaccaag cgaggatgca
7621    gatgtgatgg gactccgcat ggcttcacac gggctgcaag cacctggaag ccaaggcgtt
7681    gagggcaccc cactgccctg ggtgtcagcc cttcgcagcc caatttcttcg caqaatttact
7741    aggacagagg acttgagctc ctttctccta aaaggaaact ttgcaggtgg agtttatttc
7801    atgttaatag atggccatgt tcagtaacag ccattgcctg gctgattttt aacaacctat
7861    atttattcaa catttcatat aagtgttcca gaacagtttc attttctcct tccaaatacc
7921    tgcacttttt atttgctcta caacaaagtt gttgaaaacg caaggactct aggcttacag
7981    taaacacRaa aaatagaagag gaaaaataaa ccttcctaag tcttgttttc aagtatttat
8041    taaaacccaa ataactgaag tgactacaaa tgtcccggaa tatcagtgag ctggtctcac
8101    tctgacagac atccatgttg cagacaacag atcctcatag aactttggc tacccagaga
8161    tgccatgtga gggccccatt acatgtctaa aatccaagct ataagttcag ggtcacaggt
8221    cKgttttctc ctcgaaggaa gtacagcgaa tgcaggcctg aacattcctt agcaggtttc
8281    aggacttaa ttactcattt tcaggaaatt gcttggaaga aacatttgc tttgaatcta
8341    gctacaggaa cgcaggaccc ataaagaggt gtggtctcaa Yaggcgaccc caagaacaca
8401    atagactaaa tcctgagtca tctgacaatt cctggttgca gagctggacg ttcagtaaat
8461    ggatttcact cagactttag gccggcatgt gtcagagttc tgtccaccag cccaggtcat
8521    tctggcttttt attatatacc tctgatttat cacctcatgt taggacaaaa gaagggaggag
8581    aaggagaaag ataaggggg aaagggagag gaaggagagg aggaggagga gggagggaag
8641    agggcgagaa aaaatggaga aggagaaagg aaggacagaa gagagagaga aaggaaggag
8701    gatgggagga aggagggagg aaggaaggag aaagggaggg agggagggaa agaaagaagg
8761    aaaagaaaag aaagagagtg tattgtaaga aaatcattct gtggaaatca gaaYctaagt
8821    tctcagcacc tacattatga gggggtgttg atttccgctc ttttcatctc tgaacaatga
8881    atagatggc aggctgatta aaattctgtt tcccNgaaaa tttcaaagtc ctgagctgtt
8941    ttatctgggc agcttccact agaatttctgg agtgcggagg agaaaagctc tctcagcttc
9001    cctgagtgtc cttgctttt gttctctcct aagaagcatc aatgtaaaat gttaactgtg
9061    gcctccacaa cacatggcac ctgattatgc ctttaccaaa caccagcttt aaataagatg
9121    aacgctttgc taatgaaata gccacggaag aaaatcctgt gtggtcccgc ctcacccacg
9181    cctcgtggtt gctaatccag ccctcagttg ttccctgcag caggaagat cagtcatttct
9241    actgggacct aatgcttcag tgatgatttg gccttaactc cctggttctt gcctaatgca
9301    aatcaaactg tgaagagtgg gatttcttac ctctctattt tgaaataatt tccaacttac
9361    agaaaagcca caagataata caccaaactc ctaataccct ttgcctggtt aactctgatt
9421    gtctactggt gccaatgtac atcattttct ctgctttctc tcacacatgc tctctctctc
9481    tcaatctctg tctctctctc ccatatttat ttatgtataa catacatgca tgcatatatc
9541    catcatttttc taactaataa aaatattgtt ttataagaga caaatttatt tattggatac
9601    taaaaaagag aaaaacagat gctattattt gatcaatatt cRatccataa gttttactgc
9661    gtctaatttt ggaaatgcat acaaaataaa aaagtgatct aataaaaagt taatttgggg
9721    atactgagtg gtaaattctg ttccaaaatt ttactaagga aactcctcct caatttctaat
9781    gacaaaatgt ttgattgatt cctgttgtct tcaaagagaa taattcttga tgtttcaaat
9841    ggcatcatag catccaagcc tggtaatctc tgactatttta atgtaaagtg ttttaaaaaa
9901    aWctttggct cttgatagga caaggcacat ctttttttttt ttttttttttt tttttgggac
9961    ggaatcttgc tgtcgcccag gctggagtgc agtggcgcga tctcggctca ctgcaagctc
10021   cgcctcccag cttcacgcca ttctcctgcc tcagcctccc gagtagctgg gactgcaggc
10081   gcccgccacc acacctggct aatttttttt gtatttttag tagagacggg gtttcaccat
10141   attagccagg atggtctcga tctcctgact tcatgatcca cccgcctcag cctcccaaag
10201   tgctgggatt aaagacgtga accaccacgc ccggccaagg cacatctatt aactagaata
10261   tagcagtgca gaaaccgttt cccaaatatt atcctatggg gaaatttatct gaagatatag
10321   atatcacctc agcttcctc acttgtaccc caagtctatg ttattaaatg gcctcatcc
10381   tacaccaccc agcagcctaa gaaccaggct gcctttccca cctgtatact cctctcccta
10441   gggaaatatg ccctccaagc caccacgcgg accaagttag ggggcaatct ggcacacggc
10501   ccctacctga ggcccgtcct gccatgagcc tatcaggga gggtcctttt tcactctcct
10561   tgagatgcag taatcaccac actagaccag cacagcccat acagtagctg tggacagcRg
10621   aacctatgaa taaagcacac atttcccttg catgcttctc tgccacaaac ccatccccctg
10681   tgaatctgcc aaaaccttcc actagtctcc tcacatttta ctccaaagaa agaaacaaaa
10741   taatataaca taaatatacc ataaattcac tgtcacaata aaagaaacac tagtatttat
10801   ttatcctaaa atcatttctt cccatttttct aaagatcgaa caagttctca ttcttgttcc
```

```
10861  cttactaact tctctgtatg gaatatgggg aggaaggtta ggagctaaga acactctgaa
10921  tgacagYcac atggttctca atgtaataca tgcgcagagc aaagagagga gatccgtctg
10981  aaccctccaca tctgtgggga cacaacagaa gattcactca tgactcattc aYgtctttat
11041  ccctgcccta tacatcccta caatggaacg cccttcctcc tcaaaaacat tgcaggaaaa
11101  tgatgtcgta gatgaacact tagcaatatg gaaaactgct ctgatatttt acctggttag
11161  ttaaaaaatc acagtatata ggagaattat atccatagac tcattttgtt aaaaataaaa
11221  aggcagttgg ggatggccgt gcattctgtt ccaaagcatc tgtgaacctg aggaatagac
11281  accatgagcg aagctaacct tcccgagttg aaaaatgaaa tgcaatggtg gcagacatgt
11341  ccaaggaata ttatggggac tcgatccctt tatgaatctt gtcatagatg aatgtgtgga
11401  gatgtcaact agttggcagc agaacagtat tggaacggtg gtaatacaag gaaatagtat
11461  catcatatta gaaactttgg aatgagtata aataatggct gttcaacaga aaaacccatg
11521  tccctctcc aaagggcctg tttcactata tgtaaaaatt aggtcatgta tgttttcata
11581  ttagactttt tgttaaataa cctttttttt ttttttttt gagtctcact ctgtcgccca
11641  ggctggagtg cagtggcgtg atctcagctc actgcaagct ccgcctcctg ggctcatgcc
11701  attctccctg ctcagcctcc tgagtagctg ggactacagg tgcccgccac caccctggct
11761  aatttttgt attttagta gagacaggtt ttcaccatgt tggccaggat ggtctcgatc
11821  tcttgacctt gtgatccact cgcctcagcc tcccaaagtg ctgggattac aggcgtgagc
11881  caccacgccc ggccaataac cttttgtaat agtcaaaaaa taaaaaataa ataaaaaggc
11941  aaagtaaaaa tattgacagc tatatcttat aatacccaatg gcagagaagc tttttgtttt
12001  ttcccctctt cttctttggt tcacttatat tttcaaaaca taaatttgta ataaacataa
12061  attatatcct aatataaaaa tatgtaagta acatgcaatg ttgttcattt ttgtaaatat
12121  ctgaaaaata caggcatgtt ctgtaaaaag tgcagcccac aatacttgta ggtgtcaaac
12181  cttttagcat gcccaaatgc ctgttctttt ttaaatgtct acagcaagca tagagctctt
12241  ttttttttc atttattaa gaaaacccag aaacgctcaa gagtttcgtg gaggccatct
12301  atgcggcgat aatccattca ggtgatatta atggccttt cctgccagga actccagtgg
12361  gcactcagga agccaggatt acaggggctct atccagtcac cgcatgtctc ggcattcggg
12421  aagcctatct cagtctcctc aaattctgca cacataaaac ttcagagccc gggagcgacc
12481  catgaaacgc aggtttttaa ggacaaaaca ataggacaaa agtgctgtat attgtcctta
12541  agatgacaca tgaatttaaa atgcatagtg tttggattat tcatgagagc cccgcaagaa
12601  cgatgtccca ggggtttttg ccaggaacat gcctgagatt gatgataaga atcaagcatc
12661  tggggctgcc gcacaatgga aaactccagc actccatgga acttttccat ctgcagcagt
12721  cggaggattt gcctgagaac atacgcggca tgaagacact ctcagccctc aagggcaccc
12781  agtcaqcgct gtttaaggac ggtttttctg ttcacagcat acttcatgat tacagcttca
12841  ctccattgga tacaactatg tgagtatgtg tgtatgagtg tgtagtggtg tgtatgaggg
12901  tgtgtgtgtg gggggtagg ggagtgccat atcccccagc agcacattaa gaaataatcc
12961  aattacaatt taaataacca ttgtttcaac actttctcta agtggtgaat gtattcttca
13021  gtctcttggt tgatctgaac taatagaaac caaggaaact gttatcacat accaaatcct
13081  caacttctca acaccaagtt gcaatttcct taatactgaa gcacacgtca gttcagttct
13141  ataagctccc atggagcaat gatttcaata aacacaattt caatagcatc ccacacgttc
13201  tcaagtttag gccaattttg ctcttactca actccatatg actttaaaaa tgcaggaata
13261  ttaaaaccat tatcaaggac tccaaatagg tcaatgtatt atctgtggtt ttaagaaaga
13321  aacctaagag gagagtaatt atttgtgtac cattatttag cttaaaataa cttttaaatg
13381  tattgttcca attattaggc ttctccatat aatttggaaa ccattaaatg agtttcaact
13441  tctttgtccg tataactggg tatatctgag catagatgct acagacatca cgttgccatt
13501  ggtgcccata aggcttcgta tgcccacagg gcatataatt aagattcaca aaagcatctg
13561  actggcatcc cactctaccc ccgactcaga tccaaagtat cctttcccag gtactgtccc
13621  ctgtcaccat ccttggccaa attggagaatt tatcccaggt tgttgaaatt aattttgatt
13681  ttgattctag tcagagttta aaatgatttt ttaagaagtg tgtcaatctc acctataaga
13741  tactaaacag catcacttat ttttgtctta atctgtcact attttatgaa ttatttttaa
13801  agaaaataca gattacttct taaagaaaga tcataagtgg cactataata gcattcaatt
13861  gatagaaatt gatgtagaag cctgcattaa taatttttcc tgctgctttc taaagttggc
13921  ttttagtttt cggttgaggt gggcttttaat tcagcatcac ctcatttgat gatttattta
13981  ctaatttatt tccatcacaa atggaatcag aaatgaagcg aaggcaaaaa atctttgcca
14041  caaattcatt tatatttgca tgagtatcac caggctacct gcggatgcaa tgaagcccta
14101  tacccgtgcc tgaagtcagg agcacaggac actgggagtc tgtctcagcg cagtaactgc
14161  tacatggtac gctccacatg gtatcctctc cacctgagcc ctcctcatcc ctcgccccct
14221  ctccacacct caccctctcc acactgtatt atctcccact gcaagcaacg cagaggacac
14281  agaggtgcag ctgaagtgaa ggcaggccag ttcttttcca attcactctt atgaaaatgt
14341  gttaaatccc gttaaatgca ccgacctgaa ctgaaaYgat gatatcagta aatttgttgt
14401  tgtcatctga tgcccacaca gatctcagca catgttttgg gaaaggctgc agtgttcaag
14461  gagtactaga aatgttcttt ctgagtggac tggccatgat aagccaaaga atattatagc
14521  cgatagggat aaatcatggt tttcccactg cgcggttgcc tggtggagat tattccagcc
14581  tttatttaca gctacaaaaa taatcctgcc tcaaggattt taggaagcaa ccacctcctg
14641  cctaaagaac tacactgcat tgttgacttg ccagctagaa accagacatg agtcgtgcag
```

14701 ggaagttccc tttgaacggc ttgaattgtt gtcactagag ggtgctaaat gcccctcaaa
14761 aaggccttta gagagaatac tagtgtgcct aattcttgat ttaaattcct tgaattgaca
14821 ttattttaca aagtggtctc attttttact tgttaaaatt aagatctaac atttataatg
14881 cagaaatggt gttttttttt gaaaaatttg gattgttcat tattatagaa cataaagaaa
14941 tacacgtttt aggagcaaac atgaattaca cagatctgaa tataagatta aaggcataaa
15001 tctggggggg tgagatttgt ccatggaaat tgtataattg ttttatgcca ctgttaatga
15061 ttttaaagcc tgaaaaattt accactttac aataatttta gattgttcaa tatgttccca
15121 aatgtgagtt gcatcaaatt cggtaaatgt agagtatgtt tgttttctct gtacacaata
15181 ctgacgtcag tgctagtgcc tgcctaaact cagacaccag tagatccttt tccagaacta
15241 agtgttatag gaggaatatg gattatactg taatatatca gatgtgaaaa aagcctcacg
15301 gtcccttcct ttctcaaaaa aaacgtgtag tattttggaa tatgcatgga gtatagcact
15361 tctaaaaatg gtactttatg tatatatgaa gtaaaatagg ccttaaaact taatatacag
15421 atttccttga aaataatctt attatacatt tacactgact ttttggtcat ccaaacatta
15481 tgcacttaag caaaaagaaa tataaccaat tttgcaactt tcctcttcct gcctttgctt
15541 ctacttaaaa atatctgcag tatttccttt tctcgccgct tccactttgg ttcatatacc
15601 aaggaatYgt gaggtcaatg ggtgacagtt gtttgtctgt gttcacggct gtcgggcggg
15661 gctgggtgtg ggtaaggctc tgaccgacat ctgaagaggc ttcacccact gcggtttagg
15721 atacattttc ctctcgctct gccagtagaa cagggaggct agttttcaat gtgttctaca
15781 gaaggataat taaggcagtg tgtcacctgc tcgtctgcta tttttaaaag gaaacaaaca
15841 taacctttgc atgtgagagg cattgcaaac tagatgggag gaggcccgga ccctgtaaca
15901 gtcgtacatt ccggtcccag cttcgctSgg gtgcaactgc agataaaaga cgctggctcg
15961 acaaaaagcg cccctgggct ctgcattgcc agcatgcaca atacgaattg ctaatgatga
16021 gctggcttag gtaggaactg aggaccctga gtgcagggct aacctctgct tcacaggagg
16081 ggtccactgg cgcgcgctgg aggcggggag ccttcgtgat atttctccga agggaagagt
16141 ccatgcagca tcctgataac agggaccttg gcttcatccc caactgctcg gtgaccccga
16201 tgcgtcattt aattcatttg tgccaatatt cctttttcaa tcaaccagta actttgcagg
16261 tttgttcaaa gaagaaatta aaatgcattg gagatRgaag gcagccatct tcccggagcc
16321 ccagtgctga cactgggagg ggaaccccag gattccctca tgactgtgtc agtgatggcc
16381 ctcaacaagc acttactgaa tgagtgaatg aatgaatgaa tgaatgaatg aagccggcca
16441 cagagcccag gagtatcagg ggagagcaat actggctgtg tcagtggcta gtccaggaga
16501 gcccttcaag agcccagagt tcgacttgaa cttgggactc ccctgggatg ggtgaggttc
16561 tctcaacagc agttgacagg agggaactgg gacaggccca gccagtttca ttcagtccag
16621 ccagctgtgg ctcctcttta ggaatgtggc caggcccagc tgtggccaaa gcaccagcca
16681 gtccctcagt tctgaacaga acgtgcccag catcagtgcc ttcatttgtt tttaaactgc
16741 ctgctgacca tccacaaagt taagatgaca gctgggactt aagttgtgag gaaccagtgg
16801 ctccccccatc actctctctc acacacacgc acatgcacac acacagagac acacagacac
16861 acacacatgc acacacacag agacacacaa acacacatgc acacaaagac agacacatat
16921 aaacacacat atacacacat gcacacacat atatacacac agacacacag gcaaacacag
16981 acacacaatg gatggtatcg atatctatga acagatgaga gagagagaca gagcaggagg
17041 tcatctgctc cccacccctc ttctccccac tgtcaccacc tctctcccaa gtctagctgc
17101 aggccctgtg agctgtggaa gtggcttttt taagctgtct tcttagattg agtcattggg
17161 cagtgaggaa ggtaaatttt ctctaagaag cctcccaaat ctgtatctta tgggatttcc
17221 gtctcaataa ttgagctaat agtacctgta agcaagtgga tagtcaataa aaaaaaaata
17281 ccggctgtaa gaacgaatga atgaatgagt ggatgagtgg atgagtatac atcctctatt
17341 ttgctggcat catgattatt ttacagcaga tttatctgga tttcaatata aaataagagc
17401 tcccattgt atacaactta gtccttgtaa ttttccaaag taactctgat taaaattatt
17461 tccagccaaa ctatttaggc aactgggttg gtttcacacg tacttatcag aaaccattag
17521 aatggtatat tgattgcatt tctagacatt tgccatacca ccatggcaac tgtatttccc
17581 aagatggccc agtaggaWgt cccatcatgc ataaccttct ataaagtgac attgactttg
17641 cttccatcag aaagtgaggt ccacgttccc actccttgaa tctgagttgg gctgtgacta
17701 cagcagaagt tcagctatgt ggcttccaag gctaccttgg aaaggtgata gagcttccac
17761 ctgattttct tgggaacagc cactcttaaa cctcagccac catacgggga gaaagcccaa
17821 gccatgtgac gaggccattt gtaggtgttc cagtcatcag tcccagccca cagccagcat
17881 taacccccag aggtataaat gaagaaacca agatcactcc agccccaacc ggcacttgac
17941 tgcaaaccta taagagactc caagcaaata atatctatct cagcccaatc aagccctgga
18001 accatgagag attctaaata ataaagtgat cattgtgatt ttaagccact gagtcctgca
18061 gtgagttgtt atatagcaac cgggcatcgg cataccatca gaagattcct taagaagaaa
18121 cttttgcaac gttgctacag cagaaaatat tccttctgta tgatcattca tccattcatc
18181 aatcttgatt ggcattgcct atgtgctaag cattgtcggt cactggaggt gcagaaaaga
18241 agtgaagcag tattcagcca aacaaacaac ttgcatattg gatagagaga aaaatatgcc
18301 aaaattacaa cagtattttg acccaacaga aaggacataa gaagggaaca tcaacagttc
18361 cttcctattc ttttccaccc tttttctttc taggctcatt aaatgtagag gtgcctcagg
18421 gtcactttgc cccatgagag tagataccct cctctcccat ccctaacttt ggtcttcact
18481 ctatgcctga taccagcagc tccccaggct cctccatgct gttggcaccc cattcccatt

18541 ctctggaaac atctcagccc atcaacctca gattactttc ccaaggagat gtgagaaaac
18601 ttcaattttc ccctttgtga cttgcagaga aataggggtg gtaaatgaga agcagaggga
18661 gagggtgggg attcattacc ttgagttact aaagagaaaa gctctagtgt ttagaaggtg
18721 ctgttattat tttctctgaa acattagctc ctagaaatca gaggctctgt ccctagcatg
18781 gtctctaagg cttccaggac gccccagggg cttccctcag tcaattttga ctctaatgag
18841 agccatctgg aaggctgcaa tggtgggcct ggctgatcac tggaggggcc ttcgctgtgg
18901 gcacagggac gtgcacaggt tcacagagtg tgtctccgtt tctgggaacc atggtcctgt
18961 gtgctccttc cccaaagaaa gcaggagaaa gaaaaaccac agtcctgagt gggattctcc
19021 ccaaacatct aaaaagcttc tttaaagaag tcaagttatc ataattaaac tcacatatgg
19081 aatgcctata gacaacgtgt tgctcttcca atcccaggga gctaggacac ccaaaactca
19141 cctcccagac ggagctagga tttgagatac tggattccac attacttaaa gctgttcgag
19201 cttttcatca ggaatggaaa gcattaatgc gtctcacacg tcactctctg tttcatggaa
19261 ttcttacact gRggagctct ttttatttta ctatttttct ttaacagcca gaacactgag
19321 aagtttgcaa agaaattttt cagctgcctt tagtgaccct taactcaaga ggttttgcct
19381 aatctgtaaa ttggagttga aaatatttca gtacttttgg agtggggagc tttttgtctt
19441 taaaagagtg gaacgacact aacaataggg ctatacatac cttgtgcttc tttgtcagtt
19501 actgcaaacc aaaaccagat gtgaagtatc agcggctacc tcgtagtgac ccatggaagt
19561 tgaggctaat ccatatcatt cttaataact caaaactgcc accttttaac cacctaattt
19621 ttttctcact tacaaatgca aaaaaaggaa ttgacagtac acattgaaat cgattttccc
19681 ctgaccactt acagattttc tcctataaga gccaggaata aaagctcact ccattatatc
19741 aagcagccat catctgagta tgctttagtt taggtgatca tcacctttaa caaaccaaga
19801 tctggaagga agatttctga tctttaacaa accaagattt gaaaactaga tattcctgtc
19861 atgacctttt cccaacattc agtatgtaag ggattcactg gattattaga ctgcttgtaa
19921 atgtaagaaa acatagaagg tttagtgtga aggagttagc aacctaacaa atgtttcccc
19981 ctgaattttc aataaccttc ctgaatttaa aggtaatgaa tataaatgaa gaacaaaatc
20041 aatagatata ggaatgattc acaacctccc aaatgaataa atcRatcatt ccaccctaca
20101 tttgaacatt caatcaatat tttgtctatt tactaaatct aagaggaact actttaacat
20161 aaaactaaat atgaaattat ttccagcatt gaatattgtg ttttgcctta gagcaggcac
20221 aaagtggaat gcctatgggt acaaagctag gcattgattg atgtttaata cctacaaata
20281 cagcaattac actgtcatgc tacacgagac ttcctattcc tacactgaaa ttagactgca
20341 catatgtagg gataaaagat aagacacaat catatcatat ttcctcaaat ctaagacttt
20401 gggtggtaag atgtaaagca catcatgatt taaagtatca ctaggaaaga aaaaacaatt
20461 ctgccaatga aaattcaccg taatactttc taatcaatca attttaagat acatcccaat
20521 ttttaagcaa gaataaatgt gttaaaatta acacaaattg gtacacttgt gatacaWcag
20581 aagcactaaa atgtcacagc aatagaccac aggggtttctc aaccttggca gcatcaacat
20641 tttgggttgg ttaattatct gttgtggggg ctgccctgtg catggcagga tgtttgctag
20701 cattcctggc ctctacccac tagatgccag taacacctcg cagactccaa ttatgacaac
20761 caaaactgtc tttagacatg gccaactgtc cctaaaggtg caaccaaaaa ctgtcccagt
20821 tgagaaccac tggaacagag caattcggtt ttatcagcct tgtaatataa ttgtgtgtgt
20881 gcactgtgtg catgacagac tgtcagccta atggaaggta tattgtcaga tgggatagat
20941 tgacctgaaa aaatcacata aaccaacagc tggtacatat acaagagtgt gtcctgccca
21001 tcctaaccca cacaatgcaa aagaacctgg atgaccacga gtcaccatca caggagttta
21061 ctatccataa gtgtaaacca tccaagaaaa gtgaaaacag attaaagaaa ataaaaataa
21121 ataaaccacc acacaatatt tggcctagc cagataacaa caatgaaaaa atgtaatatt
21181 ttgaagtatt ggcaagaatg tggaggaaaa agcattgaca ttcgtgtata atgggaataa
21241 aataatttat cctttgtctc cgcaattgat attctagaaa tctatttttt agaaatactc
21301 acaatagaca gttataagta caaaggatgt ctgctattac actgctcagt aacagtaaaa
21361 tatgaaaata cactgtacgt ctttcaatca gatattgaat aattatacta cacagtatta
21421 agaatgagat agatattaat gtactgcata gaaaatattc aaagtataat aagttttaga
21481 aaattatcac atatgtatat tagcatatgc agagaaaaca tcttaaaata caaatttcag
21541 ttttgaggtt tggatcatgg agtaactgcc ccctttttcaa gtcaaacagt tgagaaaatt
21601 taggataaaa caagtgtgtg ctacctttgt aatcagataa agtattttaa aataattcac
21661 attataatat agaaatactg aaatgccaag aaaatttaaa tatattaatt aaaacctacg
21721 ggccaggcgc agtggctcac gcctgtaatc ccagcacttt gggaggccga ggcaggcgga
21781 tcatgaggtc aggagattga gaccaccctg ggcaacatgg tgaaaccctg tctctactaa
21841 aaatacaaaa attagctggg catggtggcg tgtgcctgta atcccagcta ctcaggaggc
21901 tgaggcagga gaatcgcttg aaccagggag tcggagggtg ccgtgagcca agatcatgcc
21961 actgcactcg agcctgacaa cagagtaaga ctccgtctca aaaaaaaaaa taataataat
22021 aggctaccaa ttagacttta tagaatacat aaatatatta atatagctac aaagaggttg
22081 aagcttattc attgagacaa gagtatttat tgagcatcga ctttattaaa tacactgtta
22141 gtaagataac aagtgaaact tgttaaaaaa aaagaaacta ggacaaaaga aatttgagtt
22201 gagttcccca aaaacaggga atattcagat tgtaggggaa attgggtaaa ggatttgttt
22261 cagcatgaaa ggagcaagga gcaaagaaac taaatgggag gttatgctga gaagtatatc
22321 agtatgagga aatatcttga catctacaga caaatatttg ttgccaattc attttgggca

```
22381  ttgaggattc acaagaataa ttaaaaacac gtaatataaa atccttctga ttagagcaca
22441  ttttatggca ctgcataaag agatggctgt gggagtcatt tatattttaa tactaacttg
22501  aacaaggctt ggttctgcaa ataaaacaga agagtaaata tgaagtggag cacataataa
22561  tgttactgtt tctgtgggtg agcttccata ggaaagaggc aaaggcatca atctcaaaaa
22621  gttagaaaaa cccaaaggaa gaagaagaaa aataacaaat gagaacacaaa ttgagaaaat
22681  tgtaaataat atggtagaga agataaacaa aaccaaatct ggttctctga aaagattagt
22741  tatgtgtaag tcactggtga ttacagagag aaaagaggga aggttaaaat aaccaaagtc
22801  aacaataaaa agggggctat tactacagat gctgtagaca ttggaaggat aatagaatat
22861  tatgatcaat ttcctatcaa taaatgtgaa aaattagttg aaatacataa ttggaaaata
22921  taatttacca aaactgtcaa aagaaaaaac acaaaacctg aactcctata attattaaag
22981  acattgattg aaaaatctca gacctcttaa aggacaactc caaaaataaa aaaataaaaa
23041  aaagaaagaa agttccaggc cagacggatt tatcagcaaa ttctaacatg catttaaaaa
23101  aaaaaggatg ccactcttac ataagctttt cagataaaag aaaagaaagc ttgataccaa
23161  aatgtagcta gaaaattatt taaaaaggaa aattatgggt caatttcata cataaacata
23221  gatgcaaaat cctaaataaa attctagaaa acaaaaccca acagtatata cgacaataat
23281  atatattgtg aacaaactgg atttattttа agaatgaaag cttgttttcaa tcaaataatc
23341  aaatttacat tgtaaagaaa atttatataa ctttaaacaa aagaagaaaa gcacttaata
23401  acattcaaca ttcatattaa aaattcttag taaattagaa ataaagagga agttttataa
23461  tcctacaaat tgataaaagg aatctaccga aacctacagt aaaccacaca ttttcatgtc
23521  aaaactttaa aatttaatca tttgaagttg ggggaaaaga caaagaagcc ccacatatta
23581  ccgcatttgt ctgaaattga attggcagtc ttagttagta aagaaggcaa gggaatgaaa
23641  tgcaatgtta aaggattggg aaaaagtaaa taaaacttta tttacagatg acatcatttt
23701  tttacacaga atttccaaga gaatttggaa ataagtcatt agaatttaata aatgagtttt
23761  aaaagtttgc tagatacaag gtcaatatag aattttagtt ttatatatca gcataaacat
23821  caatagaaat caaaatttttt aagtgatact gttttcatta gcattaaaaa taccttacaa
23881  tatggacata aatctaacat aatacgtgca gaacctctac acccaaaaact acaaaatatt
23941  attaaaagaa gaccaaaata aatggataga tatattcatg gattgaaaaa ctcaataatc
24001  aaaggtagaa ttttcttcaa attgatcaat agattcaatg cagatgcatt caatattcca
24061  acaaagtttt tgtgaaactt gagtgattct aaaatatgta tggaaatgca gagtcaaaaa
24121  cagacaagat gctcttaaag aagagtgaga aatacaaaag attatcagag actattacaa
24181  actggaaaac ctagaggaaa tggatacatt tctgaacaca tacaacctgc caagattgaa
24241  tcagaaagaa actgaaaact taaacagacc aataacaagt aataagattg gataggaaaa
24301  aaaatctccc aacaaagaaa agtcaaggac cagatggttt cactactaat tctaccaaac
24361  ttagaaagaa gaactaatac caatcctcac caagccattt caaaaaatta aagaggagag
24421  aattcttcct aattcattct atgaggccaa cattaccctc ataacaaaat cagacaagaa
24481  cacaacaaaa aagaaaacta caggctgata ttcctgatga acatcacttc agttcagcat
24541  ggatacaggc caatatttct ggtgaatata agttttctag tattttgttc agcaaaagct
24601  atcaacaaaa tattagtagc ctgaaaccca cagcacatca aaagatatat gcaccatggt
24661  caagtgggat gtatcccaga gatgcaagga tggttcaaca tacacaaatc aataaatatg
24721  atacatcaca tcaatagaaa aaaacaaaaa ccatatgatc atatcaataa atgcagaaaa
24781  ggcatctgat aaaacttaac attgtttcat agtaaaagct ctcaacaaac taggtacaga
24841  agaaacatac ctcaatatat taaagtccat acatgattaa cccacagcta acattatact
24901  gaacggggaa aggcggaaag tctctcctct aagaactgga acaagacaag gattctcatt
24961  tttatcactt ctattcaata taggactgga agtcttagcc agagcaatca ggcaagagaa
25021  agcaataaag gtcatccaaa ctggaaaaga agtcaaattg tccctctttg gagtgacgat
25081  gatcttacat ctagaaaaac ctacagactc caccaaaaaa ctcttaggtt taattaaaaa
25141  attcagtaaa gttgcaggat acaaaaaaat cagtagcatt tatataccca ataatgcact
25201  ggctgagaaa gaaatcaaga agaaaatccc atttacaata ggtataagga aaaaatatct
25261  aggaaaaaaa ttaaccaagg aagcgaaaaa tctctacaaa aaaactacaa aacactaatg
25321  aaagaaatgg aaaaggacac aaacaaatga aaagacactg catggtcatg gatcagaaga
25381  actaatatca ttaaaatgac cacaccaccc aaataaatct acagattcaa tgcaatccct
25441  gttaaaatat taacgtcatt tttcacaaga atagaaaaaa acaatcctaa aatttatatg
25501  aaagcaaaaa ggagcctgaa tagctaaagg aaccctgaac aaaaacaaca aaactgggag
25561  catcactaca cctgacttca aaatatatta caaggctcta gtaaccaaaa gagcatgata
25621  ctagtataaa aacagacgca tagaccaatg gaacagaatt gataacccag aaataaatcc
25681  acatattcac agccaaccga ctttcaacaa aggcatcagt aacatacatt gggaaaaaga
25741  caccctcttc aataaatggt gctggaataa ttggatatcc atatgcgaaa gaataaaact
25801  ggacctctat ctcttgccat atataaaaat caactcaagg tagatgaaag acttaaactt
25861  aagaccccaa attataaaac tattaaaaga aaatagagaa aacatttcag gacattgatc
25921  taagcaaaga tttgatggct aagacctcaa aagcacaggc aagagaaaac agacaaatga
25981  gactatatta aactaaaaca ctctctgcaca gcaaaggaaa gaaaacaacc agcagagtga
26041  agagacaacc tgttgaatgg gataaaatat ttgtaaactg ttcatctagt aagagaaaat
26101  ccagaatata cacaaaactc aacaactca acaattaaaa agaaaacttt tacaaagtgg
26161  gcaaagaacg tcaatagaca tttctcaaaa gaagacacag gaatggccat caagcatatg
```

26221 aaaaaaaata ctcaatatca ctaatcatca gggaaatgca aatcaaaacc acaatgagat
26281 atcatcatac cttagttaga atggcaatta ttaaaaagac aaaaaataac agatgctggc
26341 cagaatgcag agaaaaggga actcttctac actgtgagtg ggaatgtaaa ttagtacagc
26401 cactatagaa aacagtagag atttctcaaa aaactaaaaa taagactcaa tataatccag
26461 atatctcact actgggtatt tatctaatga aaaagaaatc agtatatcaa aaagatactt
26521 gcacccacat gtttaccgca gcactattta ccatagcaaa gacatgaaat caacctaaat
26581 gtccatccac agatgaaatg gtaaacaaaa tgtggtacat atacacaatg gaatactatt
26641 tggccataaa aataaggaaa tcatgtcact tgcagcaaca tggatggaac cggaggtcat
26701 tatgtcaagt aaaataagcc aagcacaaag gacaaatacc acatgttctc actcctatgt
26761 gggagctaaa aatgttaatg tcatggagat agagagtgga atgatggtta ccagaggctg
26821 agcagagagt gggagtggag aggaagagag tttggataat gggtacaaac atacagttag
26881 atagaaggaa taagttctga tgttgtatag cagagtagct gactatactt aacaaaaatg
26941 tattgtatag ttcaaatcag ctagaaaaga ggacttgcaa tgttcctgac acatagaaat
27001 gagaaatacc caaggtgaca gacaccccaa aaccctgact tgatcattac acattctatg
27061 catgtaacaa actatcacat gtaccccata actatgtgtg tgtgtgtatc tatctatcta
27121 tctatctatc tatctatcta tctatctatc tatctatcta tttatagtat ccatttttaa
27181 aaggcaaatc ttaaaaaaaa gagtgaggta ggacaacctg ctctactaaa catttttata
27241 aaggcacagc aattaggtca gaatagtgtt catgcaggta gaaacaaatc agacaatgga
27301 aaagaaagga aagttcagaa acagattcac acatatatgg acacacttga tttttgacga
27361 aggtggcagt tgattttttt ttacaaaggg gcagagtagt taaaaaaggg agaaactgtt
27421 ggtaaatgat gctggaaaat gagaaatcca catgagaaac agaaacttga gaagtaactc
27481 ataacatcac aaaaattgat gtcagataaa ctataaatct aaatatgaca agcaaaaact
27541 atgaagtttc tggaacataa tatagaaaac tatattcctg acttgggaag ggaaagattt
27601 taaaaacaag gcacagaaac actaagagta aaggaaagac taataaattg aactgcatta
27661 aaataagaaa aaaattagga acttaaattt tcatcaaaag acactattaa gagaatcaaa
27721 aggcaatgca tggagtggaa gatgatatct ttaacacatc taatctacta ttcatatcca
27781 gaatatgtaa agaaccccca tcaatcaata agaatacaca caagtcagaa tacacacaag
27841 gaaaaacagg gaagaaactg cacaggcagt cataaaagag gatatccaac tgctcattaa
27901 aaggtcttct acttcattag taaagcagga agtacaaatt aaaacctgaa tgaaataaca
27961 ccacagatac atcagaatgt ctaaaacaaa gactaacaat gttggtgaag atgtggagca
28021 ataagaactc tcacacacag ctggagttta Raaaacatcc ttatttatcc atcagggctg
28081 taataagagg catatagcat attcaaatag gtaagtgaac aaaatttaat gaaagaattt
28141 acaacggtaa aggtagaatt tagtaaaaac caaagggtga ggaagtcccc caggctagca
28201 agaacaggaa gccattacta ccctcaggcc tacaagggca agggaggtag cagtcacgca
28261 gcaccggtag ctgtgaacac aggagaggat aaacaatagg agctgtggcc ttccatggag
28321 ggaaaaagtc actgccaacc catgaccaaa gagagaaagc tggagaaaaa aactccccaa
28381 gctctctcct cctactctca ggcttccttg tggtgactct catttgctta acccaacaga
28441 agatagagga caaaggagcc catttgatgt agtcgacaga agtcaaactc ccaggacaag
28501 aggagcagag aaggatggag aatgaattag agaagtaaac aaagaaagtc ggcacatcta
28561 ctgtcatcaa agactgtgta attccactat ttaatacatg tacaatagag atgtgtgtat
28621 atgtgcacca gaagtcacct acaagaatgt ccactgcagt attattctct cagttaaatg
28681 ctatatctgg ctgcacaact agattaggac tgagacccta accacacatg tagaagcagg
28741 gagaaagatg cagttgagaa gccctttgcc atctgatatg cttccaaaca agggaaactc
28801 agcttggaca ctgaaagcat tttgtataaa atactgtttg tatgatatcc ccatgtcacc
28861 acacacacac acatacagac acacacacat acacacacac acaacaaaaa caaaaaaaac
28921 ttccagggtt actttctcc tcagttagca ggtcaaaact tttcacgtgt gaaatacttt
28981 tgcaaggagg cagatgaaac gggggagaag ggataacctt gccttgcagt catctatcaa
29041 ttcactgcaa ggaaggaaca cagagcttag atatgaagca tcaggagttc ttcccaagac
29101 ccttcttgtc ccttgggaag agccaggagc tggaggggat ggccttcact gagaagtggc
29161 atcaaattag aacctgcaca acaaatagga accagctact taaagatcca gagaagtagc
29221 cctctagact gaaggatcag ctcctcaaat atccttttg attttgaact cacaagttca
29281 ggggcatccg aggaacagac acaagccagg gctgaacaat ctcatctgtg tccatgaggt
29341 gggcaagagc cagatcctac tgaggagttt gaacttaatc ccaaacatgg cgggaagcca
29401 ttggggccaa agatgaatta gggattgtct gatctccttg acacgttctg aaggttttgt
29461 gtacaRaaaa ggtttgtcaa catgcacaaa ggaaagctgg gataaccaag ctaagacgct
29521 accgcatcaY tctaggggac gggtgactca ttccaggagt ttctgcagga agacctatca
29581 ggactggtga ttgactggag gcagagagca cgaaaaaaga acaatcagag atgatctgtg
29641 gtttgtggtt gttgtgtaat gttaaggctt aacaactgcg aaaatagtgt ttttacttta
29701 cagagaagaa gacttgaaga atacaagatt ggggagagca gatcgggatt tgtactttat
29761 atcagacgtg ctcatagata tacatgttga gatatcagtt gggagctgga tatatcagga
29821 ttcgagactg ggaatcacca gtttatagat ggtttttaag ccatgtgatt ggatctcatt
29881 tcttagtggg gagaagtgag ataacaaata aaagccaaga ttaaagctga accttcagcc
29941 tgcccatcac ttagaagccc agcagggaca gaagagccag ccgacaRcac agagtcgagg
30001 aggaggattt cYgggcttca gtgagtgtgc atcagagatt catggacaca acttaaagta

```
30061  agaccagcca cacagttccc ttcattttct caagcaacat tcagcatctc aaagtgcggc
30121  tactacacac ggagccaagc cctggtccag ttatcacaaa accttactag atatgtcgat
30181  tattagctgc attttatagc taaaggtagg caggcacaga gaagttacgt ctcttgccca
30241  cagtcacagc aagcaaacag acctcagacc aaagtctttc taactcctta tttcacatct
30301  aaaacactat gtgacgccac cKccaaaaaa tgtgggggtt actctaggac aaaagaagct
30361  catgaaagca aagagagaag catagagctt aaatttagaa caatattcag ggtgattggg
30421  aaaaatagcc tccatacaaa tataatcggt tcatcaccag gtgaataaaa tgagagagga
30481  acctggtaca agtgaagttc attgaatttg cttgcaaaaa aacataattc aagtgtggaa
30541  gtttggaaac taaaatagta atcagctaaa gaaatttcca ggccaactta gacacaatgg
30601  tgacaaagct cccctgagga gacaggaact atactacttg caactctaac tgaatggact
30661  taacttagca attaagatca ccgtaagttt gatcagataa gtattaaagg gtgtcttggg
30721  tacatttgca gattcagaca ctcttagttg tgaaattctt caccaaaaat ttgcaactta
30781  tggcttgcac attaaaaaca tgatatgaat gaaattcaga tatctcttgg taaattttat
30841  aattattcct cccatcagct aaagttctca gtatgaaggg ttataactga tgtcatatac
30901  aataactaca agctgtatca tacaaaaatt gagaattttc tattatagaa agagttgctt
30961  taatctaaac ctaaagtagc atcaataatt tttcgtaagt ggtccccttc ctatgagtaa
31021  gcccccagga aaaataaatt gcttttaaga aatgctgtaa gtaagctgtt tcatatataa
31081  gttttgacaa gatctggcta cttaaattac aagatataaa atgagatttg tactttttct
31141  caaatgtaaa aaaaaagatt tacttctgaa ataatggtct ttataaaata tgcatttttg
31201  ttccttttc ttatcatatc tataaattta ctaataaaag attctatctt gatttactaa
31261  catttgaaaa gattgattat attggtattg caagaagagg ataccataaa ttaaaaatcc
31321  atatattaac catattcttt tatttgcaat atgacaaatg attgtgtaaa gttataatca
31381  ataaaagcta tttgaaagtc ataaaatgga tattgccata actgctttcc tagcaaggtt
31441  aaaacacttt aactattttt aatcaactta cagtgtagta gatcaagcat atctaaatat
31501  tttattttaa tcaagcaaat atatttctgc tgttcctatg acagtatgaa agtttggttc
31561  aaaatatttc caaggtattt aacacagttc agtagaggtc ctgtctcata aatcaatttc
31621  agattagata aaaggaaaaa gcaaattctt gtttacttca gaatttttca agccagttcc
31681  aaagacagag ttgttactct catgtgaatt ttcagtagaa agctgaacaa cgacgttgct
31741  ctgacaatct ttttaaatac catatgatgg agacagaata acaaaaacaa agtaggtata
31801  agctgtacga aattatttct cttggacata aaatatgttt ggggaagaaa tgcattgttc
31861  catatggact agggtagtta cttctcaaag tgggagcaac tcagactctg aaaaatggtt
31921  tctcaaagga ggcattgtgt ctgggtgagg ccagttttct agtcaaaatc attttattaa
31981  atgccattgg attgaatgct tccaggtttg ctctctgaaa tatgccctat cattcttaaa
32041  aaacacactt aggtagcaaa aagggcacac taaaaataac gtgggttaat gtttctatcc
32101  tgcctgtgtt ttctaagtag cccctgcctg agctttcgac tttttaaat gaaccatcaa
32161  atagttggtt gtctatcaca aataagccat ctattttgtt attcctgtaa cttttYgtag
32221  aatccagaaa gtaacattct tgctgatata tcttatataa caccaagtcc attttccaaa
32281  tgaggattcc aatgagtatt catcaccaac atctccccga aaaatattta gaaaaaacag
32341  actcaatcct ttatccaaag tcagtgagta agaggcgggg gccagggttg gacaaaaatc
32401  tctttggcca ggaagccggt ggtcaccctg atctacttct ctaagctccc acccctgatg
32461  aatgttcaat atctgagttt caccccactc attattgtaa ttctccgtaa aacccYagtt
32521  acccacacgg aattctcatc tacRtctagc ccaatttgct actggatttc aatgttattt
32581  catatgaaaa caatcactaa cagaaagaac ctggatctgg tttcgaaaac ataatttgaa
32641  aggaattcat tctgaaggct gcaaaagccc agtgatggcc catcggtacc ctgaatgggc
32701  ttctcaggtg cctccactct cctccgtatg tctccatcca tctcaRaata catgtctggc
32761  tcttcctgct cataaacaga aacagagagt tccgggatcc aaaggcaaga ctgcgattta
32821  agagacactt tgtttttgta ggtgttcaag gatttggaat caaagcagca gaattattaa
32881  aattaatcca attttcttgc atttattttg ttagttcata cctctaaaag atatattttg
32941  gaaggcaccc ttcaacccac ccatttacaa atcaaagctt tctttggaat ccctgagacc
33001  aaacccaagc tagacagtga cacactgcca gctccagagc cctgcccacc tggaaggggt
33061  atggaatgca ctatttgact tgagctcaca tttaattaca gtgtcaaaaa tcaaacttaa
33121  attgctttaa tcagctKcca acactatgag cctttctggc ttgaatttct ataaacaaag
33181  aataaattca aatctgtcac aaagtggcag caacttgttg accactggac taggaatcgt
33241  tatgcaacca tggctcactg tggaaaaagt caacatcttc ctatatgtga ctcttttctg
33301  atcttttcgg actattagtc aacagaatca tcataaagct aaattatcta tctgcactga
33361  aattactcag cctcagacat ccaaaccagt agctgttcac caatgaaacc tgaataaagc
33421  tgttgctgac tttccctgct tcaatttaga gtatttttgg aaacatcatt gcatgtttaa
33481  aatataataa gcaaaaggac ctttggtaat taaacattct gtaatttaaa actccaaRag
33541  acaggagcag tgataagata ttagattttc tttactgggg tgaaaaagac agaaagtggt
33601  taactgttta aaaaaagaaa gaaagaaaga aatccaagga tttttagagc cagaaacagt
33661  aacagtgtcc tttattctgg aaatgtttaa aagcctgtaa gcagagatca cccagttcat
33721  cctgagcatt ggtgagcaaa taacttctga aatgctcttg aaagagaatt ctccagcctt
33781  ctctgtttga aatacttYct aMagcaaaca caaaagtggg caaaacacaa gagctcatgt
33841  taattccaaa caaagagacc aacagtcgca aattgagagt ccatcttaga agcgggtgct
```

33901 gcttccacat caagcaacta ttggaaagag taggggtaga tgcagaatta agatcatttg
33961 tgaYtacaga aagagacaag aaaattaatt tttaaaacta aaagagaaat ttatttcaga
34021 taatccaagg aaatgagcag agtcaaccta acaggatttct caagccctc cctactggtg
34081 tggtgtgaag atcacacgtg gtgtagctga cacccctcac atcttcccg cRcccctcct
34141 gccacctctt tttggcattc accctctctc gggttctgta tccctgccca tgttctccat
34201 gaaagccaY gttaatgccc atgctctttc ctgcctctaa cagacgatgc cttccacagt
34261 cactcaagct ttaaccctct tctggattcg gacctgtaca tccaaaagcc tgccagRcat
34321 ctcttccaga tgctctcaga gcacatgacc agaagcacgc gcaaggctct cctgagcctc
34381 agtgctttcc ctccaacact tcttccactc tctcagttac cgagccaaga cacagagttg
34441 cttgtgagtc atttctctac ctcatccccc acccaacctt cctgctcaYg
34501 ttacctccta aatgctgtta cgtgacttca accacgtcag ctttttatgg gggaggagag
34561 gcacctgcat atctgtggga gcaccaacct ctagacatct cctgccaagt tactgcaatg
34621 tgcagaaaag aggaagaaag caagcccaag tcgcaaagtc tttgccagtc cttctaccaa
34681 ccacaccttc ggtggagatg tgggtctgtg gaaatgcaga gacggactga aagccaaatg
34741 ggccaatgag agMtctgaac aaaacattaa gcttgttttt ctttaaggca atacgattaa
34801 cagtggtcca ttaaggatcc gtttaaaaaa aataataata atacYtttct tgactgatgt
34861 tggggaagaa taactccttt atgggggagta tgaactcaaa gacatgatat tgtaaaaggag
34921 gccttgaaga agagagggac taagaaatgt gatggcgtgg tctgttacat gtgcaggtgc
34981 tgtgtgtgag ggaagcactg aggaccactg gaggatgagg gatgctctgt ccttctcggg
35041 tatggctgaa ggacagggat tgcccatcaa ggagtaaata atccatgagt ggactaaatt
35101 ctttagaaac aggaactcaa atccagtagg gattaggata aaaatgtaaa ctctaatttg
35161 cacctctccc tctctcccct aagtagtccg tttctataat tttatactaa atcaattaaa
35221 tgtatctgct ataatattaa tcataatttt gtctgaagta gtaacaactg ggaactacct
35281 aaaagagtca gagcaggact gtaagactat attgtagtct acactatgtc acagYggact
35341 gcatcatgat agagaacgat actcatgatt taactgataa acacatatgg caatgaataa
35401 aactgtgagt aagatgtctt taattttagc aaaattatct tcatttctaat tttcaagtaa
35461 acttaaagat ttatatataa atgcacataa tttaattaaa atacatgcat atatttaacta
35521 gaaggctaat cccccaaaat gtccatagat gttatttctg agtgaggagg gtcaggaagg
35581 ttttaatttt ctttgtacta actctattta ctaaaatgtc cacctggatt aacgttataa
35641 taaaaatgtt accgttaaa ataaaatgaa taaaatacac cggtatgaag gtattattag
35701 aacatacgaa agtacaaaat caagcagcaa aaggaggaaa ttatattaag aactgaaaaa
35761 actatgttga gaattctgtc taagaaacgc tgtagcaatt aagaaaaatc ccagttctgc
35821 aagtaatggg agaaagatga tgacttccag aactttcacc atctactaag atgttcacca
35881 attcctaaga agggactgaa tacgtctgca tcctcagatc tgagagtaat tttccacgac
35941 gcatactgag caccataatg agtgaagtct ctgagatgac ctctctgacc tctctaaaac
36001 aatcaggcac tgcaaacatg gcctatccca cactagccct tggtgaaatt caagggcata
36061 atattagact gaaacagtga gaagaagatt cgacatggag tgcggcaaga atgtgttcta
36121 gtccttgaag gccagcgcta ttccaagtgt ggtctcagac cagcagcctc agctgcagct
36181 ggggcttgg aaatggaaac gtatgtgcct cgtcctggac ctgtggaatc agaatctctg
36241 aggtggacca ggaatctgtg tttttaaaac cctgtggttg gtaacttcct gctggctgag
36301 gacagagaga atgcttagtg aacgctgagg aatgacgggt taaataatcc ctgaatgatt
36361 cctgagcgga tcaatttctc agccagagtt ttgaccgcag ctgatgatga acagggctgt
36421 gaYcaccagg aagggtctga agaggaggcR ttgattgcag ttttctgcct ctgatcctca
36481 Kgcatggagc cccacccccc aactctctta cacggaggcc aaagaaaaag ctggaattct
36541 ccaggagagc aggacctgtt aaacagcaaa gggcaaccca aaattgtatg agtggccttg
36601 ccctgagaag ctttgaagcc agaggttact gaacaactac cctggttaaa accctaacgt
36661 gacaatgata acatgtgact gtatgtggct gtcttcaaaa cagcaatgat ttaggcacaa
36721 ctgtggatct cagattgttc cgtgagtttg gtctgataag attgtatgcg tttcccaggg
36781 gtgccataac aaagtgccac accctgggcg gcttccgcca ccgaaatgta tttctctcaca
36841 gctctgaggt cgaaagtcca agatccaaggt gtcagcaggg ctggttcctt ttgaggctgt
36901 gagggaggat ctgttctagg ctctctctcc cccagcttct gggggctgct gcagtctttg
36961 gtgttccttg gcttatagaa gcatcatccc aatctctgct tttgcgttca catgtgcttc
37021 tcctcatata cctgtctgtc tccaaatttc ctcttctcat aaggacacca agcactggat
37081 taggggccca ccctactaca tctgcaataa ccctatttcc aaataaggtc acatttggag
37141 ggaccagcta aatacaaaac attagccagg catggtggtg ggcacctgta gttccagcta
37201 ctcaggagaa tcacttgaac ctggattaga acttcacaat tactgacacg attcaaccca
37261 tattaggttg tttagtatta tacattagga agccatagca aactttttt ttttttttt
37321 ttttttttt tttttgagac ggagtctcgc tctgtcgccc aggctggagt gcagtggcgg
37381 gatctcggct cactgcaagc tccgcctccc gggttcacgc cattctccctg cctcagcctc
37441 ccaagtagct gggactacag gcacccgcca ctacgcccgg ctaattttttt tgtatttttta
37501 gtagagacgg ggtttcacct tgttagccag gatggtctcg atctcctgac ctcatgatcc
37561 acccgcctcg gcctcccaaa gtgctgggat tacaggcgtg agccaccgcg cccggcccat
37621 agcaaacttt tgtaaacata actatttatt aaaatttggt ataattaata tttaaatatc
37681 ctttctggca agatttagcc agttttttaa gcttcattga gagaaccaca atattagcat

37741 taataataga atggtctatt aattttttaa aaagatacta tgtctgcatt tccaatataa
37801 aattcacagc aatgattcag gtagaaatta aatgaggatg tcattgtcaa ccttttaaat
37861 tatattacag gagcagggag cacacgggcc ctgaggtaga aatgaataag gaatattcta
37921 gaaccaccaa gaagccagtg tggccacagc agagtgagcc agtggtgctg gaggcaggtg
37981 agatcttgaa gggccttggc aacatgaaca ggagcttgga ttttatccac attgccgagg
38041 gaagtatgag gtggtgttta gcagggcata aatctcatct gatctgtact ttgaggaaaa
38101 cactctgact tctgtgtgga gaacagtcta taggaagcca agaggagagg cagggagatg
38161 agggaggggt gacttcagtc tccaggagaa tgagctagtg atgtgaatta aggtgctggt
38221 ggtggaggaa gtgaggtgga gaactggaca ctgggatcta ttttgaagag ggagcctaca
38281 gaacttgttg gtggatggct atgagggaaa gaggattaaa gaatgatgct aggcatttgg
38341 gcttaaacaa acccctgagt aaatggttat cctattatta atactaagat gggtaatgct
38401 agggaaggag tagccttggg gagcagtgat gagttatttt cttagaSaga agccacgtta
38461 cctataggag gctcaacaga gtatcaaatt agaataaaat atctaatgtt ctgatttgtg
38521 tctttatttt ttccattaag atacacatgg ctggccaggc gcggtggctc atgcctgtaa
38581 tcccagcact ttgggaggct gaggcaggcc gatcacctga ggtcaggagt ttgagaccag
38641 cctggccaac gtggtgttac cccgtctgta ttaaaaatac aaaatattag ccaggcatgg
38701 tggtgggcac ctgtagttcc agctactcag gaggctgagg taggagaatc acttgaaccc
38761 aggaggcaga agttgcagtg aacYgagatc acgccattgc actccagcct gggtgacaag
38821 agcgaaactc cgtctcaaaa ataaaaataa acaaaaacca tgggaaagaa caattgagga
38881 aactggggac ttgtcctgga acagaagaca cgaggacttt tggtttttta gttttgtttt
38941 tgtttttgag acagagtctt gctctgttgc ctgagctgga gtgcaatggt gcgaactcag
39001 ctcactgcaa cctccgcctc ctgtattcaa gtgattctcc cacctttgcc tcctgagtag
39061 ctgagactat aggcgcacac caccatgccc agctaatttt tgcattttta gtagagagag
39121 ggtttcatcg tgttggccag gctgtcctca aactcctgac ctcaagtgat ccacccgcct
39181 cggcctccca aagtgccggg attgcagaag tgagccactg cgtccagcaa gaatgaggtt
39241 tgaagggagg catgattgtg ttctcttcaa atagttgaaa ggttccattt gaaaaaggga
39301 tttacttatt cctatggttc tagtaagttg cagagggtgg atctaagacc attgggtgaa
39361 ctttacagag aggccagaaa gccttcWcca ggggaagaaa gtcaagaaaa ggtctcaaaa
39421 ctgtctggca gaattctgca caggagagtc ctcaattYgg tgtagaattg gcaagtataa
39481 taactgtaaa tccctctcaa tctaccatct acatcattag gcgacatctt catttcctga
39541 aaattccaac acatgaaggc tcacttacta tcaagatgag caagtttgtg ctacatagtg
39601 aatttgattt caataggact cattttatac cttttaagag tctttaaaac gttgaaaatg
39661 taaagatctg caagagcaac tgatcttcaa agtcccgtcg agtcacagga ttttgtaatg
39721 atgtctaaag aggaaaattc ccatttcaga aaaggctcaa tagtatttaa tagttagctc
39781 aaaaggacga ataaagttct acatgggaag ctgctgaact aSagtcaggc caaaccttca
39841 tactcggaga agatgactgg gcctgtagac acagatattg atgataaatc atcacaaacc
39901 acagctttcc ttaattgggg tggtgggcag ggagagcagg cttcaggttg gccttcctcc
39961 agcaagggca cacacacaaa ggggacctga acacgtggag cttatggtca ggaagcctga
40021 agtgcctgac ccagcacatc tggtgactag tagtgtagat tccccacaga aggaatgaca
40081 aggcgtcatt attcaaagtg accttccctc cattggaata atcagaaaca gctcacaaat
40141 aaagtaatct gtaagatgct tcatcttctc taggtaacct ctccccaaca tgatgacatc
40201 acttcacatg aggcgacatg gttttgtgag gacttttctt tccttccaag tttggaatct
40261 ggctgaaggc taaaatcacc atttacagtg tttgagccct ccttSacact ttgaagaagg
40321 gtctgtgtaa atagccattc ctacttctca gactcgccag aggcaaaacc tgttttgctt
40381 tggtagtaca cgctcttcct taactggtaa aagactttaa aaaaaaataa gatgccattt
40441 ttaattgttt cataaatctg gcttagatat attaaggaaa ttgctatttt atatgtagaa
40501 cagcggcaag caaatctcaa gagattaaaa atcatgttct tgtggttttc ttttagaagc
40561 tgcaaatttg aattcaattt aaaaaatcat ggcacaggga caaaataaga atgaacaaag
40621 atgggaaaaa tgtccgcagc attctgcaga gtcaagcgct gctgtgagtg agtgtgcatg
40681 tttccaatta cacatcaggg cttggcgagc tccaggagtc aaattcagac agaacccaag
40741 tgcagtgcgt tacacagaac ccaggccagg aaaagcttca cagagtcttt ctttcaactg
40801 aggcaattgt gtagacaatt tggttcattt caagaaaaaa ataaaactga cagaagaaag
40861 aaaaatatYa ttatattttg cctctcaaaa caaagtcaaa ttgtgttggt gtataaatca
40921 agattYagta tttccttggc tgcttccaga ataatagtag atcacaaaga gaataagaac
40981 aagaaagttc agttctcagc cagacgatcY aaggtaacaa agggtgagac cctcattccg
41041 ttactcacag gagcaaacag acaaccaata ataattgggc acatgggggt ttcaacaaga
41101 taaactgtta tgtgagtcca gggtgctaat ttcYggattc ttttgagttg caaggaaaat
41161 atataccgat tccccacccc cacccaccca cataacaaga cacaatagtt aacagctgga
41221 agactgtggt taggggggaaa tgtgattgta ggcttccatt tcaaatgatg gaaaatcatt
41281 tctgaagtca ctacgaaagt tacttcacaa aactaaaaga agccttgaca ccttgtgtta
41341 tcccatcatc taaagcaatt ctagtttgga aacacttgat tcttggcagg ggattctaaa
41401 gaaggtgccg tatgtgaaag gctggtgtgt cagaaggagc tttaaggaac tggaatgaga
41461 acagccaaaa gctaagattt ctgattataa tcacaggtct ggatgtgttc aaggtaaaaa
41521 gagatcatcc ccatcatttg caatattttc aagagaatgg ggctttagtg acactgatca

41581 aagtctgaca tggattttca gctgccttcc aactccacat acctgcaatt caatgatctc
41641 tatggatagt agaagtaact gccaccctga tgttctcatc ggtgatttat acgtgaagtg
41701 gactcaaaag aaatacaacg aaatcccttа ataaaaatta tgtccattga cccaacaagc
41761 ttcccagtgc tgtatcagtt ctcaaccgat tttagagaca tttggtcaaa aatgatctac
41821 ttgtaataag ccatctgagg gcactagctc tttttcacct ctgtgttcct tgaagcagga
41881 agtcagtaaa atcactattg aattaaaatg aagtaaagca ctttgagatt tcagatttct
41941 aaattaagga acacacaaca tacggtactt tatttgcaca agaRttatta gaaccCaggg
42001 ctaacaccca aatgaggtca caggtaaatg aaaatctgtc tcagttattt gaactcaggt
42061 caacacacag acagagcaaa gcaccagctg acctctgatg cacaacccag tgttcttacc
42121 atagaattcc agaaggcatc tcagtcattc tcttatgtaa atacaaagac gWcaactggt
42181 ttaaaaattc atttatttttt attttagctt ctttgtgtca aactcaaaga agcctcacat
42241 aaatgatcaa agacttttтg gtggatcttc caaacgtaca tgccgggaag gcctgcttgc
42301 acttttтcct tcaatcctct aaaatgaagg ttttgaagat gcttgccaat ggaacgttgt
42361 gccttacagc tataatattt tttaaaaggc attcagttta aattaatata tttggccaga
42421 caactgtatt aaaattgttg ttgtttttтc tgttataatg gtagcctgtg gtatgactag
42481 tcttcttcaa aaatatgtac agttattgct tctctcttgc ctgggtata tcatgtgttt
42541 ttcatttgag tgtacattgc aatacctcat taaaaccaac acttaggcta cacaaaagtc
42601 ttcatatcat gccgcaaagg gcgtaaacta acgtggaaag tttcagagcc tcataactca
42661 ttgcatatac ctcttatact agctgctcaa ctgatattta gctctcctgg atgatgtcac
42721 agttttatc ctcttaaaat agcctgcctt caKaaaatat atagtttcct tcatgcacta
42781 atcatgggga gttacgatgt aaatagagcc atttttttc ttatacaagg aacaagtgct
42841 ctcaccctcc tcccttctct ccctccccat acacagaagc acacttcact tcacttatac
42901 taaacacttc acttatactt acactgcaac aaagagttgc aaatacatgc aaataaagcc
42961 tttatаactc ccctctctcc tgctggacag ctccttgact caagtatttc Ygaagacaga
43021 cactctgata agggtctgct ctgagcttca ttctcagcat acagtcctgg gattatttac
43081 ctcaccaatat tcacctctgc atgaaccagt aagtcattac tgacaagaaa aaaacaattt
43141 gtgatttttt ttaatgtcac aatttttctt tttaaRgttt gggagagaaa gttgttttga
43201 atgtttcatc agtttctatt gccaaatgaa cacctgtttc agagtccctg aaagtcacac
43261 atcagaagct tctgacttca acatatagtc tgctttgaag aattatttta aaaaagcatK
43321 gactgcttga agataagcaa gtgacactca atagcttcat tctttagtct tagaaaataa
43381 Wttttacact tcacacctat taggatggct actatgaaat ataaaaaaaa ttaaaaataa
43441 caatggtggc aaaaatatga agaaattaga acccttgtgc actgctggtg ggaatatcaa
43501 atgatacagc ctctatggaa aacagtatgg tggctcctca aaaaattaaa aatagaatta
43561 ccatatgatc cagcaattct acttctgggt atatattcaa aaaaatttaa agcaggatct
43621 caaagagttc tttgtacagc catgttcatg gcagcattac tcacaatagc caaaaggtca
43681 aagcaaccca atcgtccatc cacagatgaa tgaataaaca aaatgtggca tacaataaaa
43741 tgtcattcag tctttaaaaa gaagaaaatt tggacacatt gtacaatata gatgaatctt
43801 tttttaaatt aaagtggttt ttttaatcgt ttatatttaa agtccgagg cgactatgca
43861 ggatgtgcag gtgtgttaca taggtaaacg tgtgccatgg tggtttgctg cacctatcaa
43921 cccatcacct aggtattaag cccagtatgt attagctatt ttccctaagg ctctcccacc
43981 cccaccatcc cccaacatac accatagatg aatcttaagg acattatgct gcgtgaaata
44041 aaccagtcac aaaaagacaa acagtgtatg attctactta tgtgaggtac ctagagtagt
44101 ccaagttcag aaagtagtaa taatggttgc caaaaggtgg gRgcatgcag aacacgggga
44161 gtgttgattg acatcaagtt tctgttttgc aaggtaaaga agttccagag atttgctgca
44221 ccaacaatgt gaatatactt aacactactg aactgtaaag tggttgtgac tacagatttt
44281 atgttttatg tgtttgccac aaccaaaaat aaagattaaa ttaaaaaata aaagatttta
44341 tagcacctat cacttaccaa acccactgta catcttacac tcRtgaatat tttatgattt
44401 tcaaaacacc tttatttttt tcccttattt gttcattcct tcatgtataa cccacaatgt
44461 gttaggttat gtgctgggca gcctggaaga cccaaagacg aattagggaa gtaccctata
44521 tttaaagcct tgcaaggaca taaatatcag taatattaag taaaatatgt tcactgctga
44581 aaactgctat acttcctaga tttttcaatt caattgcaat ttctaatatt ttgccatgtt
44641 gatcccacaa attcacttgt gtttaaaagt taacgtgctt gattatcata cagctgcttc
44701 tttcataaga ggaatacaga taaaaYgcta tgggatttca gggggagaaa gaacttctta
44761 ttaaattcat attttcaacc aataagaaaa cacaattttt tttaatcaac actatcttct
44821 tggtgctttt ttcacatctc atcctctttc ctcctttacc ctgcctaagc aaccatttct
44881 ggacccaatc ttgggttatt acatctgacg gcaagtgtta tgtgggccat ggaccatgag
44941 caattagccc cctctctact cctagggatg gagtacatgt gatgatttcc atcagactca
45001 gattaaatat cttgctggta agttacccct aaaaatcgat taatggactc tccaggtaga
45061 cactgaggta atctccaacc aaacctRact tatacttagg ggctttggaa gcccaccaga
45121 gtcatcaagc catatctcca Yctaggctct aatctggaaa gctggtcagt agtaacacaa
45181 agaacaagcc atttgggaaa acagcccaca tgaaaagaac tgtggtttca agaaggagtca
45241 ttccatccca ggtttaaaat actcttctcc tctttatcta ccttgaggac tcctatctat
45301 ccttccatac cagatccagc ctcatcttct aagtgaagcc ctcctctggg acgtcagcSt
45361 ctcctctgca tcccctagca ttttatgcat cctctgttaa agcaactgtt tgcacagctg

45421 Yatccaccac taaacttaga ggcaacagac catggYtttg aatgtgYaga acccaacaca
45481 gagccYgaga cctagtgggt attcagtgca tgttgaaggg aagaatgaat gcatgagcaa
45541 acaagacaat ggaagtctgt catcagtatt tacatttcaa aatgcaaagt gaaaattgtg
45601 caaatctcta atcaagctgt actttaaaat gctaaattga tttggctaaa aatatttcaa
45661 cactgaaatt tctttttgca agttaagtct tcgcataacc aaaacagaRa agaacRtatc
45721 aatgaactaa atagataaat ttatggctga caaaatctca agatttagtg tgtgagagga
45781 aagtaaaatt caatgtgtcc ttgaaagttc tggggtctaa gatatacagg ccaatggaat
45841 agaatagaga cttcagaaat aaactattgc atatatggtc tgataacttt tgaaagtggt
45901 tcaaagatca tttaatgaga aaaaaaggag tcttttcaac aactggtgtt gggaaaactg
45961 ggtatacata tgcaaaagaa aaaagttggg ctcttacctt atactatata caaaaattaa
46021 ctcaaaatag aacaaagacc aaaaaataaa agctaaaact ctaaaattct tatgagaaaa
46081 ctctaaaatg cttagggaat aacttcataa cactggattt cacaagcctg tcttgaatat
46141 gacaccaaaa gcacaggcaa cataaataaa agagacaaat ttgcctgcac taaaattaaa
46201 cacttttgtg agtcaaacaa gctatcaaca aagtcaaaag acatcctata aaataagaga
46261 aaatatctga aaataattta tctaataagg gattaatatc cagaaaaaaa aatatatata
46321 tatatgtata taacctacaa ctcaacaaca acaacaaaaa caacccaatt taaaaatggg
46381 caaaggactt gaacagaatt ttttccaaag ataacactaa tggccaataa gtacatgaaa
46441 ttatgctcaa catcactaat cattgggaaa atgcaactca aatccacaat gaaatacttc
46501 gtagccatta gtatgactat taccaaaaaa tcagaaaatt acaagtgctg gtggagatat
46561 ggaaaagttg caaatcttat gcactggtgg tgggagagta aaatgggaaa gtcactataa
46621 aaaacagtct agtgattcaa aaattaaaaa tagaattaac atatgattca ccaattccgc
46681 atgaagatag caggaaattg aactgatatt tgcacatcca tgttcatagc agcattattt
46741 acaataacca aaaggtggag gcaacccaag tgtccatcca cagatgagtg gataaacaaa
46801 atgtgatata cacatatcat gggatatctt cagccttaga aaaggagaga aattctgaca
46861 tatgctataa cacagatgga cctttggaaa gttaagagat tgtcttattt atcttacgct
46921 aagagaaata agccatccac aaaaggacaa atgctgtacg attccacttg tgtgagttac
46981 ctagggcagt caaattcaca gaaacagaaa gtaaaatgat ggtttccagg ggctgagaga
47041 agggtagaat ggaaagctat tgtttaatgg gttggagtgt cagtgtaaga aaatgaaaaa
47101 agttctggag atggatgatg gtgagttttg caccacaatg tgaatgtatt taataccact
47161 caactgtaca ctaaaaaatg gttaggatga taaattttat gtatatttta ctataacaaa
47221 aagtcataaa aatcaaacat ggttcttctc attaaaaaaa aaagaagatt cctgggtcta
47281 gttggttctc cctccttctt agttcttgga tcaaggagat agaattgtgt ccaaagtgac
47341 caagtgacct acggagtaat gggcttccat ctagccactc cctgctttat gactgagctg
47401 cactgggaga ggcattgtca ggggaaattc caggtttcta gaattggtat ctagccagaa
47461 tttgtcccag ggctaagtgg ctaaggcagt gaactagtct gtcagcttct ctgttttaaa
47521 tggagtcatg taattccatt acataccctt tgctttcaac tatatggcca aacatgactg
47581 gccagcaggc tgggggacag aagacatgtg ggcttgtgct tgttaYctgg aattgaaaag
47641 agctcttggc atggttcttg ttcaagctcc atggttgact agcacatgac caccaagaga
47701 gctactgtac ttctccgaga ctcattttct cttctgtaaa aaatgactga gtttctttca
47761 cagtgcataa atcttttcct ccaggaacag agactgccca gggcctgtcc aagacaacta
47821 ggaaaccaga gcagcagtta agccattcct gggcaggaat aaatgagcag atgtcagctc
47881 tcagaatctc agtttctca ctcataaaat ggaaaagaat actatttctt ttatgtcatt
47941 caccatattg tgagctgaag gcactttaac gatgctgagg ctgtaaacta atgcataatg
48001 tgatgtttat cattcttcac ctatgtttta gttactgagc atctcctgac accagagagg
48061 acgcaacaaa aatcacaact cctagaactg cacagtctaa atggcaacca ctagcccctg
48121 tgacaactga tcacttgaaa agtgagtagt ccaaattaag atgtgctgta ggtgcaaaat
48181 atatgctgga tttggaagat gttctatgaa aaaagtatct cattagtcat ttttatattg
48241 attacatatt aaaaagattc cattttggct atgctggact cttcagatat atcctgggag
48301 attgtattaa aagaaaatac atgatggaaa ttagtgtagg tagttactag aaaatgtaaa
48361 attacatgat tcacatccta tgttcactgt tctagacata taaatataac tttgagttat
48421 ttttaagcat gagaagacag aaatcgacga ataaagtgaa aaagctaaag attaaagata
48481 cttacaaatc attgttgtat tttttaagag gtcattttga gcatattcct taccattgaa
48541 gcccctgcct gtctggctcc tctgcccacc ttgttttgct aatgggtcat gctcctatat
48601 gtgcatagac gaggagcggc tctcagggac tgaccgtaag catagtcagc acagcacgta
48661 tacccatgct ctgaccccag gttggcgtct tggagggtga agcattttcc cagtccttct
48721 ttgactcatc acagaggtat aaaacagcgt ctccaacacg tgattttttt tttttttttt
48781 ttttgagaca gagtcttgct ctgtcgccca ggctggagta cagtggcacg atcttggctc
48841 actgcaacct ccaactccca ggttcaatca attctcctac ctcagcctcc caagtagctg
48901 aaattacagg cacacaccac cacgcctggc taatttttgt attttagtag atacggggtt
48961 tcacaatgtt ggccaggctg gtctcaaact cccgacctca agtgatccac ccatcttggc
49021 ctcccaaagt gctgggatta caggctgagc cactgtgcca gttaaaagaa aaaaaatatt
49081 caaacatatt tggtttctta ttgaggtgaa gttcacataa catgaaacta acagttttaa
49141 agtgaacaat tcagtagcat ttaattaaca atgttgtcca accaacacct ctgtctagtt
49201 ccaaacattt ttgtcacccc aaaaggaaac cacgtgctca gaaggcagtc actccacatc

```
49261  acccctcttc ctagtcctat gctttgcaca caactgactc accctgacag ttataaccta
49321  aaagttaaat aaaattatta gtaaactgca aacccctggc aagtgaatta cttaatatct
49381  cttaaaatcc tgacatcaaa tgattcccct gtRagccaat gagatgataa gaacatccac
49441  ctccctctct tgctccagtg gaatgaaacc ccctcctcaa ggagggttac actcaggcat
49501  aggcccgatc actcatcata tattgacaga tgtgcaggcc tgagacccca ccttctggag
49561  cttttaatg ctccttgttt ctcaatccaa tccttgctag gaattaggct cttctgctga
49621  atgtaaaatt tttccatctg cctccataaa gtatgtgcca cctgtcagct gactggtcaa
49681  ccccaagctc aaagtatatg gacatttgg gggtgacaat ggtgggcata catctttagc
49741  aaagattaag aaggtaccag aggaggacca gcacaaccca gcaatgcagc agaatYcatc
49801  aggaaagctt tggctctggg tggagctcct tgctttagct ctgccttgga gcgcttgggt
49861  ggctggggag gcactggggt ggaagggaag gaagcaggaa ttcgtgtgct gcaaatttca
49921  ctacacttga ccacaacttg gagtggaaag ggcactgtgg tRcgtctatc tggcctcct
49981  ttacaagcct taaaatgctg tggaatccat ctggatggaa gacgccatcc aattataaat
50041  ccttaggata ctttttattg ccctttaaga gttcYgatgc ttgctcttcc atRcccatat
50101  gtttctgctt aagaggcttc attcaaatca aattggaaga gaagtccaga ttaccccaact
50161  acaattacct gagcaaaaat cccctcaatt atcttggtaa tccagataaa ttcggagtac
50221  aaagtgtagt tgcctggata gcactggcta agaactgctt tgtctcccat ttcagccttgc
50281  attattataa tctacttgat tacacttcat ttataacaat agggagggct tgttttatgc
50341  cacacattgc cacttgctca agtgtaaaat aaaccttaaa tgactgatgt actgctaaat
50401  ttatctcaaa aaacaatcat aacaggaatc ttaaggcaat aaagtcaaac aaatagaatt
50461  ttacagaatt taaaaattat tttgtgagtg atttatgcta aaataacctca aatttatttc
50521  aaaaacagtc ttacttaaaa ctgacttaaa atatatgtag gataaataat Ytgtagtgaa
50581  tttaacgaaa cttcagcaat tcaaatgaat gcacRttatt cttcttaaaa acagatatcc
50641  tgaaaatatc catcaggata aatagctaat gcatgtgtgg cctaatatct aggtgatggg
50701  ttgatagagtg cagggaacca ccatggcaca tgtttacctg tgtaacaaac ctgcacatcc
50761  ggcacatata tcctggaacR taaaattaaa ttaaatttt aaaaagcaga tatttggaaa
50821  gtaccaatag cttcaaagta aaaatactct Ncactgtttt tgtttgttta tttattttcg
50881  ttttgtattt tcttttttga gatggagtct cgctctgttg cccaggctgg agtgcagtgg
50941  cgtgttctca gcttaccaca accttctgcct cctgggttca agtgattctc ctgactYggc
51001  cgtgccacca tgcccagcta attttttttac attttggtga gagatgatgg ggtttcactg
51061  tgttggccag gctggtctcg aactcctgac ctcgtgatcc acccgcctca gcctcccaaa
51121  gtgctgggat tacaggcgtg agtcaccgcg cctggcctat gcactgttaa ttttatcacg
51181  acagttataa atccatcaag atgtcctgtg atttttcaac acaaattact caaattatga
51241  acttctctgt gtgtattttc cactggcttg tttatgaatc ctgctgatat gtctgctaca
51301  atttctccaa aggctaaaag atgtttacag gacaaatgac atcatgacca tgtcaggctt
51361  aaatgtgttt atatcagttg ggtttagagg gtcttcaaaa catggcttta aaatctcagt
51421  tattatggag cttaatgtgt tcctgatgtt tctggagtMa tgtatttcta aaaatagaga
51481  aatagattgg ttaaaagaaa atgaattgtt ggtctaatct gtcttatgca tggctaacga
51541  aatgcatttt cactctctc cgtgatatta cgacactaa aactgtgagg accaatcggg
51601  tgataagaga caaaataaac agtaaatata tactccatgt gagttactac tctgtaatag
51661  atagaaaaga tattttatag aaaagggaaa atacccacag acatataagc aatgtcctgt
51721  ggttgctatc aaatttactg ttagctgttt aaaactgcct taaaggtttt ttaaatgtgt
51781  cttttctacc atagattctt tagacgacag ccatcaagca gcaatacctt cgcaggaggc
51841  cattgtgttt ctatttgaac ttctatggat gtcaagctct gttcttcaaa atttagccct
51901  acagatgggt ggcccaccgg agagaattaa tctcactatg cagccaacac taccctttct
51961  ggatctttcc ccagtagtgt ggattctgct ctagtccaga attatgcaga ataagtatac
52021  ttcatcttag acaccataat tcttcaaata tctaaaatgt attattgctc ctccaaatcc
52081  tggtcatctc caggttaagt atctctcaaa aacagtccat cagataatat gattttaaat
52141  ctttatcccc ttggtcatat acccacaatc tcattctatt taccaatatc cctactgatg
52201  cataaactac atatgtatat gtgtgttttt tttaaaaaa aaagcaattc cactgtaatt
52261  ttagcagagg ttatttccac atagagctat gtatatgtgt atatacacat atcttatat
52321  tatatagttt tctgtgcttt cccagttatc tacaatgggc atatatgact ttttatagcca
52381  ggtaattcaa tattcattca ttcagtgaac atcattgagc atccactatg ggctgggaag
52441  tgaggatgga gccacaaaca agcaaaatag aaacccctgc tcttgtggag ttcccttctc
52501  attggaagag acgtacagta aagaaaaaaa taaaagagta aagttaatag cctgtgagaa
52561  ggggatataa aagtgggaag gaagacaggg tgatgtgtga gaaacacttt ttttttttt
52621  ttttcagatg aagtctcact ctgttgccca ggctggaggg cagtggctcg atctcagctc
52681  actgcaacct ccacctcctg gtttcaagca gttctcctgc ctcagcctcc caagtagctg
52741  ggactt cagg catgccacac catgcctagc taatttttat atttttagta gagacaggat
52801  ttcaccatgt tggccaggct ggtcgtctca aacttctgac ctcaagtgat ctgcctgcct
52861  tgacctccga aagtgctggg actacagcaa tgagctgcca agccccggcct ggggaacact
52921  attgaatagt gtggtcaggg aaggctttac tgtgaaggtg atgaagaccc aaagaaagtg
52981  agaaactaag tcatcaaatga tgggtagaac attccggatt gcgggagcag caagtgcaaa
53041  ggccctgggg tgaggaatac caagaatgtt tgtgtgggca gagcagaaag aaccaagggt
```

53101 aaagcattag gagatgaggc tgaagaagta accgggatca ggtggttagg gccctcaggc
53161 cctggaggaa ggctggcagc gctggagcca caYggactga caatgtctag cagtcatccc
53221 ggctccctgt gaagaacaga ccctcgcttg cagagaagcg aggacaatta ggaaagcaga
53281 gtcatgatcc acgcacagga tcacggtgac ttggaccaga aagagagcag tggagctggg
53341 gagtgactct tttcagtatt tctcaggtgg taccagtggg atctgcagag aatacatagt
53401 taaaggaaat gtctggaact aaacatgact cttcaaacgt gatcctactg tggcagaaga
53461 gaggcgactt tacatttcct ttcccaggat atcttattct aatgaacaca gaaaccgtaa
53521 aatcaagcca accaacatga tgaaaatgat tatataaggt acacagccca ggctggattt
53581 gaactgatga gggaaaaaaa atctctagtg aaaattcctc tctctaacca cagccttctc
53641 tccttccatc tctgcctcac ccttgctctt tctgaagcct tcctggatgc tcatgaagct
53701 cYctccttct ttgactcatc ctattttccc aggacMttta tcaactcagg gctcttctcc
53761 cctccccaca gtcagctcac tgtgctctga ctagYtccct gaaattgctc atcctcttac
53821 taaccaggaa gcttctaccc gctcttggtc ttctttctcc accccagtgc caaagaacta
53881 agcactgatg gagaaaaagc atgcggctaa tactgtctgt ctctaccaca aatctcataa
53941 tttttaaaat ccatttggaa tttacattca ctccttaact tcttttcatt cactcctaat
54001 tcacttccta tataattctc tacacagctg ctgaaaacct tcctttctgc tgcctcttac
54061 cccaaaacta ctctcacatt actcacaaag gttgaccttg ttttctatWt actttttttag
54121 agtaaYgaag ccataaaatg taagttcttt caacctggac ctcccactct tgggatttct
54181 caatagcttc acctgtattc tccccccttca ctcttgactc agaggtaaaM gctcccttgc
54241 tcccaaatcc tttagcaacg tagggttgat aattgctcct ttccaaattt aatccctgca
54301 tctgcgcccc tgagacagac actgccatga tttcccagct tgctgtcttc tccctcctgc
54361 atctcctccc tttctctgtg acggatattt tccctgtgca agagaaattt cttctgccct
54421 aaaataaata atccaaaaca tctcttgact ccacttaagc taacattcaa tatctcactt
54481 tcccttgtat taacaaaagt taattgagtc agtacggtgc tacaattctc agacacaacg
54541 ataaacatga tagagaccat caacatgcct tggcattttg cctgctttct cttcaattac
54601 ttgcaacttg gcttctactg agctccactg aaaaagcttt catgacatga ccacatccaa
54661 tcccaaagaa actgtcccct tgcccagtgg tcttcaaaac cctccaactc cacagtgtct
54721 cattaactcc aactcatttc ctactaaaca tctcttctca gctcttcaaa gtcaaagatt
54781 gcgaaccaaa tctacagact tctcctctct tctcctttgg gtccaactcc atccttctcc
54841 atgaaacttc ttattcctag aaatggtgtc tgcacctttt aggcttccag gctYgagcct
54901 agagtcatct ttaactcttt ccatacccag actcccaaga cccagtcagc tgtttaggtg
54961 tctcctctgt atgcagcact tactgtcatt gccctggtcc atctcccaga gcccacatct
55021 tgtcccactg tctgcaaagc ctttcctata tgctggatat aagtgcaaac tccccctaaa
55081 atcccattga agtttttact tttttctatc ttcttttttt acttcttttt atcttcctct
55141 actcacacag aagtgctcca attatgagga ccttatttta ttccctttac tgtcaaacac
55201 aaagccaaca tgccatacga aaagatagta ctgtgcttcc ttcagtgcca ctctagcacg
55261 cccactccag cacacccttc ttgtgcgggt gtatgctcat gtgatactat cacaggcaac
55321 acttactatg caatacgttt tccacaatca caatatttcc acaatattgt gatatgagct
55381 cattcttcag gccttgacac aagcgcccac aaacctaaga gaatgcattt tcatttttat
55441 gatacacagt tttcRactgc tccactctgg ctgccaaggc attcctcctc caaatcacRa
55501 tgtctatatc aaaagaagaa caatgaggga gagctggagg tagcgctaag aaacaacctg
55561 gtccagctcc caggtctcat agagaacact cagaacacgc ttgttagagg tatctgctcc
55621 tggcctcagc ttctcagaag caattacaca tcttctgggt aaacgtggag tgtgcagcac
55681 agaataccaa agctgagctt cccattgtac ctggttgttg atctcctcgt tgacctccct
55741 cagctgaata tttcttaaga acagtgttca attaatccaa ctatccctgg tggctggcag
55801 gatgaatcag ttatgactta tttcatgttt gtgggtgggt gtatgaagtg gtcctcaaag
55861 gagattttttg ctctctgcag acagtctgcc tgtctgtagg tcacttcctg ccatttcctt
55921 tgagtgggaa tatgagccag ggtgttggaa gaaggaagag tccaaaagat gtctcaggga
55981 atgtcccata gccattggcc tggtctgccc tagataactt ctgagccagg tcaccctaaa
56041 gtgctacatg aaaagtcatg gatttttttt ctaacttgtt gatctcaaat gtcgtgattt
56101 ggcatgaata tctagcttcc catgttgcag ctatggattt attcttgcca aaatattggg
56161 gattgggctg gagagggaag aaggtacgaa gatgcattct gtgttgctca acaagatctg
56221 catggcctca accaatgcgt gtttgaccat atggatattt acaaacccca ccatcaactc
56281 accaaaatga agagtgtctt agacttattc tcacaagaca agagggaacg ctgcctctaa
56341 ggagtctctc tgggacacct gggagagatt tatttaatgg taaagcaagg aaaggaaaag
56401 atgaacagtg acctgcaaat cattaaagag ggcgactcga tcataggcaa gggcttttat
56461 tagtgctaaa attccacttc aaagtttgct gattcatgga tgctttttgt tttgctgttt
56521 aYgttgtaga aactgatttg attttcatag acaaaataac taggcattta taaccacata
56581 taggtatgaa agaaagataa aatgatgccc ttagcccagt cagaaatact cttaaccatc
56641 aaaatagttc cctgaatcta aYaggccaac aatattccaa caccagaacc tttgctacca
56701 tagccagaat ttttaagact gcaccactgt taagtagagg caatttttaa tacttagggt
56761 ctaaccacaa ggcataaaat gcaaaaaaaa ttacataatc ctgtactttt taataattaa
56821 atgaaaatac atagactcta agcaggaaaa tatctgagat ccttaaaacg gtataatcat
56881 aattgttcta cattggtaat atgtgtgatg atatttttct ccaaaaaaaa ttctctacca

```
56941   tttcattctc tttRatttct tctagcccgt aaggtctagc aaagaggaat acctgaaaag
57001   atgcaaattg taccctgtg ctgttcaatg acagcaaaaa ttgcagctcc ccaaccccac
57061   ctcttatgtc ccctgagcaa tctgtgatca cttgagggtg aggacagtat attgccccaa
57121   taaactggct ttccaccaag taccaccaag aaatcaaaac agcttttatt ttattgtgtc
57181   atcatatata agttaatagt tcataattag ttcaaaattt aaaattatgt tctaaaaata
57241   aagctttcta agtcaatgta ggcaacRatt ccaagatcct tatagttttc ctctcttaaa
57301   cagagaccat tatcatatga ttttttttttt tttttgagac ggaagctcac tctgttgccc
57361   aggctggagt gcagtggtgc gatctctgct cactgcaagc tctgcctcct gggttcacgc
57421   cattctcctg cctcagcctc ccaagtagct gggactagag gcacccgcca ccacgcccgg
57481   ctaatttttt ttttttttt ttttttgca ttttagtaa agaccacgtt tgaccgtgtt
57541   agccaggatg gtctcgatct cctgacctca tgatctgcca gccttaacct cccaaagtgc
57601   tgagattaca ggcgtgagcc accgtgcctg gccagtcata tgatttctaa agagaaactg
57661   aacagttatt tgtagaaact ctgcaaagca tgactttggg acgggcacag tggctcacgc
57721   ctgtaatccc agcactttgg gaggctgagg cgggcagatc acgaggtcgg gagatcgaga
57781   ccatcctggc taacatggtg aaaccccgcc tctactaaaa aaatacaaaa aaattagcca
57841   ggcatggtgg tgggcgcctg tagtcccagc tacttgggag gctgaggcag gagaatggcg
57901   tgaacccagg aggcggagct tgcagtgagc caagatcgca ccactgcact ccagcctggg
57961   caacagagca agactctgtc tcaaaaaaca aaacaaaaca acaaaacaaa acaaaacaaa
58021   aaagccatgc ccaagcccac ccctgaccag tgaaatctcc gggattgggg cacaggtata
58081   atgtttttat aaacatcttc ctagatgttt cctgcatcca gggtgataaa tcatcatact
58141   aaaggcatca tctgaaggct cctagagtat agagaagttc agaataagga ccccaaacta
58201   ttgcacatcc tgacactaac tagctgtagc tgtgcaccct ggacagggag agatctaaac
58261   agctagttat cttacttcac cRaaatctac aactaagaat gtgttatcac gtgttatagc
58321   tttggcttcc ctaatctaga tgttcaatct acttttctgc aatttggcaa agtaaaacac
58381   acatatacag taatgcacaa tgtcctgatt gttgggttt attatttgtt ttgcatttac
58441   gcttcttagg tatggacaat gccaaagtca tgggagctga gtctttgaa acagaggctt
58501   ctttgggtgc aaatattaat tttctatgaa aaaaagagaa agtacaaaga aaagaaaaaa
58561   cagcagtaat acagaaatga atatcttcct tgtctaggac acagtgtttt ttttaaccta
58621   gatttctttg aacacagact gacacaaaaa ttaaatacta ttgctccatt ggagaggtgc
58681   aaacctggag cggtgagagt gaggggaagc gagtgaagtt gtcactacac tagcttctgg
58741   ggacatggag acagccagtc actgagcccc tgccttccct tggccatgca gatgcctctg
58801   atagggtaca cggaaaaatt ctacctcaca gcagcccatg gggtggagga aaaataggaa
58861   cttagttgcc tacattcttc ctgcatcccc ttcctcattg gtcagagtca ccctgMatgt
58921   ctgggttgtc acctgctccc aaggtgacca ctccaaaagt caggttctac gccggtggt
58981   ggggtgcttc atccaagtac agaaatgcca agaggatccg gaaacctttt gacctggttg
59041   ctgagtcaca ggaaagaagg gccagccctc ctgggacagg taacaggctg gccctgagct
59101   gtggaagccc tcacaccgag aaggagtcaa tctgctgggg tggccactga gaccaagcag
59161   gagctgaggg tcctggagta atagatggag gcccatgaga tgtgttcaga cacatagtgt
59221   gtttgtcaac tgcaatgtgt gtgtgccccc aaaattcatg ggtttaaatc cttacccca
59281   aggtagcagt atgaggagga ggggcctttg gaaggtgact aggtcataag gatggaggtc
59341   tcatgaattg cattagtacc tttacaaaag ggcacccagg gagattccct ccacctttg
59401   tcacagtgtg aagacccagc aagaagatgg acatctatga atcaggaaga gagccctcac
59461   cagaacccaa ccctgctaca ctctgatctc agacttccag cctttagaac tgtgagaaat
59521   aagtttctgt tgtttatatg ccaStcaatg tatagcactt tgttacagca gcccaagcta
59581   agacagccta ttatgtatga gcaggtggct ttgagataat tgagaaaaca gagactataa
59641   ctacaaccag ccagagatgg gatcaYtgca aatgggactc gggttcacac aaggtttgtg
59701   acacacacac aaaaaaacat aaggcagata aatcagcaag ggtagcagtc aggaattgac
59761   agacgattaa tggattgagg aaacagaata gataatttaa aagcaaacct ttgtacacaa
59821   aagaatccag gaggtgataa aagtaacatt ttcatatcag ttggaaagta agttattcca
59881   tagcaacaga acaatcattt attgaggaaa aaWaactatt tctttcctgg ttcaatcttg
59941   gggtgttgta tgtttccata aatttatccc ttttttttctg ggttttctaa tttttgtgca
60001   cagaaatgtt ttttaatagt ctctgaggtt ttttttttat ttctgtgggt tcagtggtaa
60061   tgtccccttt gtcatttctg attatgctta tttggatctt ctctcttttt tctttatcag
60121   tctagctagt tgtctatcaa tcttatttat tctttcaaaa aaccaacttt tatttttgtt
60181   ggtcttttgc atggtttttt tgtatctcaa tttcattcag ttcagccccg attttggtta
60241   tttcttttct tctgctagca gtaagtttgg tttgctcttg ttttttctag ttcctccagg
60301   tgtgacatta ggctgttaat ttaagatctt tccaacttttt tgatatcagt gtttagtgct
60361   ataaacttttc ctgttaacat tgctttaact gtatcccaga gattctggta tggtgtatct
60421   ttgttttcat ttgtttcaaa taatttattg atttctgtct tagttttcatt gtttacccaa
60481   aagtcattca ggagcaggtt gttcaatttc catgattttg agagatattc ttagcattga
60541   tttatatttt accgtgctgt ggtctgaaag tacggctagt atgatttcag ggttttttct
60601   catttgttgc aaattgtttt atagccaagt gcgtagtcaa ttttgaagta tgtgccacgt
60661   gtaagtgaaa agaatgcata ttgtgtcgtt gttgggtgca gtgttctgga gatgttcttt
60721   aggtccattt ggtcaagtgt caagtttagg tctcaaatat gttaagttag ttttctgcct
```

60781 tgatgatcta tctaatactg tcagtgagat gttgaaatct cccactatta ttgtatggtt
60841 atctaagtct ctcactaggt ccctaaaact tgatttatga atctgagtgc tccagcattg
60901 ggtgcataca tatctagaac agttaagtct tcttgttgaa ttggaccctt tatcattata
60961 taatgccctt ctttgtcttt tttgatcatt gttggtttaa agtctgaaat tgaaacgctg
61021 aacagaccaa taacgaatta caaaattaaa tcagtaatat aaagactacc aaccagaaaa
61081 agccctagac cagagagatt cacaaccaaa ttctaccaga tgtataacaa agagctacta
61141 ccaatcctac tgaaactatt acaaaagatt taggaggaaa gactcctcct taacctcatt
61201 ttatgaggcc agtatcattt tgatacagaa acctggcaga gacacaatаa gaaaagaaac
61261 ttcaggccaa tattcatgat gaacagggat ttggaaatcc tcaacaaaat accagtaaac
61321 caaatccagt accacatcaa aaagctaatc caccatgatt aactacacat tattcctggg
61381 atgcaaggtt ggctcaacat atgcagatca ataaatgtga ttcatcccat aaacagaact
61441 aaacacaaaa accacatgat catctcaata gctgcagaaa agacttccaa taaaattcaa
61501 catcctttca tgtttaaaac actgacaaac taggcattga aagaacatac ctcaaaatac
61561 taacagccat ctatgacaaa cccacagcaa cactgtactg aacaggaaaa gctggaagca
61621 ttccccatga gaattgaaac aagctaagga tgcccactct caccactctt agtcaatata
61681 gtactggaag tcctagccag agcaatcaag caagagaaaa aaaaaaaaaa gaaacaaaat
61741 acatccaaat gggaagagag gaagtcaaac tatctctctt cacagaggac gtgatttatg
61801 tctggaaaac ctcattgtat ctgtctaaaa actcctggat ctgaaaaaca atttcacaac
61861 gttttaggat acaaaatcaa tgtacaaaaa tcagtagcat ttctaaacat caacaatgtc
61921 caagctgaga gccatatcaa gaatgcaatt ccattcaaaa tagcaacaaa aaaaatacaa
61981 tacttaaggg tacagataac tggggagtga aaatctctat gacaagtatt acaaagctaa
62041 gatcaaagaa atcagagatg acacaaagaa atggaaaaac attccatgcc catggatagg
62101 aagaatcaat attgttaaaa tggccatact tcccaaagca acttatagat taatgctat
62161 ttctatcata ttactaatta cattttcaca gaattagaaa aaactatttg gaaattcata
62221 tggaaccaca gaagagccta aatagccaaa gcaattctag gaaaccaaaa agctgaagta
62281 tcacactacc tagcttcaaa ctatgccata aggccacagt aaccaagaca gcatagaact
62341 agtacaaaaa cagacacata aaccaatgga ctagattaga gaacccagaa gtaatgtcac
62401 acatctatag tcatctaatc ttcaacaaag tagacaaaac aagcaatgtg gaaaggattc
62461 cctattcaat aaatagtgct tggataacta gctagccata tgcagaagat tgaaactaga
62521 ctctttcatt ttaccatata caaaaatcaa ctcaagatgg attaaagact taaatgtaaa
62581 tcatacaact ataaaaacct agaagaaaac ctagaacata ccattctgga cataggccct
62641 ggcaagattt tcatgacaga ctccaaaagc aatggcaaca aaaacagaaa ttagcaaatg
62701 ggacctaatt aaactaaaga gcttctgcac agcaaaagaa actatcaata gagtatacag
62761 acaatgtaca gaataggaga aaatatttgc aaattatgca tccaacaaag gtcataatag
62821 cagaatctat aaaaaaaaac ttaagcaaat taacaagcaa aaaacaactt ctttaaaaaa
62881 aatgggccaa aaaaacatga aaagcacctt ctcaaaagaa gacatgtgtg accaacaagc
62941 atatgaaaaa acgctcaaca tcactaatca ctagagaaaa gcaaaccaaa accaccatga
63001 gatatcatgg cacaccagtc agaacggcaa tttaaaagt caaaaaataa cacatgttgg
63061 tgaggctgca gagaaaagg aacagttata tgctgcgtgt gtgaatgtaa attagttcag
63121 acactgtgga aagcagtttg gagatttccc aaagaactta aaatagaact accattcaac
63181 ccaataatcc catcactggg tatataaagg aatataaatt gttctactgt aaagacacct
63241 gcattattca cagcattatt cacaatagca aagacataga accaatctag aagtccatca
63301 gtggtggact ggataaagaa aaaaatgtgg tacacaaaca ttacagaata ctacacagcc
63361 ataaaataga atgaaatcat gtcctttgca gtaacatgaa tggagctgga ggccattatc
63421 ctaagggagt taacacagga gcggaaaacc aaatatccaa tgttttcact tataagtggg
63481 agctaaacac tgagcacaca tggacacaaa gaatggaatg atagacacca ggggctgctt
63541 gagggtggag ggtagacgaa gggtgaagat tgaaaaacta ccaattgggc actatgctta
63601 ttacatggtt tatgaaataa tctgcacacc aaactctcat ggcatgcaat ttacccacgt
63661 aacaaacgta cacgtgtacc cccgaacctа aaataaagt tagaaggga aaaaaaaaaa
63721 ctaaatccct atctcacatt atacatctaa aaaatccaaa tagatagat ttaattaaaa
63781 attaaaccat aaaacacaga aagaaaatac agatgaatag ttatataatt taggatgaga
63841 acagcctctg tcaggatgaa ctaaagaatt cacaaaaaaa aatgttaaca aattaaatga
63901 catgttaaaa atctggccag gggtagtggt tcacacctgt aatcccagca ctttgggatg
63961 ctgaggcggg cggattacct gaggtcagga gtttgagacc agcctggcca acatagtgaa
64021 acctcgtctc tactgaaagt acaaaaatta tccaggcatg gtggcacacg cctgtaatcc
64081 cagctactca ggaggctgag gcaggagaat tgcttgagcc cgggagacgg aggctgcagt
64141 gagctgagat catgccactg cactccagcc tggctgacag agggagactc tgtctcaaaa
64201 aaaaaaaatt aagaaactat atattgaaag actataaaaa atagttttgg ttttttctc
64261 agtaaaaaaa taatatatcc attgtcaaaa attttctatt ttcaatatta ttatttaata
64321 gaaaaatttc aacaatttct ggagaaaata tatgaaacac attttgacaga gttttaacat
64381 ccttaacata aaggatgtaa cttatatgtt acatcctaa catаatttc tttgttcagt
64441 taacaagttt ttattgagta tctatattga aatatgcact atgtctgaca ctggcaacac
64501 atttgaggaa ataaagaaga aaaattcaag tccacatgga aaaatggact aaggacatga
64561 aaaagtataa atcatcagta cacttctaat aaagttaata atcaaagaaa tgcaaataaa

64621 tgtgacctat caaggtcttg ctatttgtac tgtcaaatta taaaaataca ataacaaata
64681 ttggcagata ttggggaaac aagtaatgtc atatactggt atgtgcttaa actggtaaaa
64741 gtcttcagaa aggaaattgg aaatatatgt aaaaatttg gacagttgca tattctttgt
64801 tctagaaatt ctacttatat gattagaacc taaggaagtt atcatagatt taatcaaaga
64861 tagttacagg atatttcaaca tagccctgta tataacagcc aagaatctga agccaacaaa
64921 aaatatttag cttaaaatgt atagaatata catggatga aattgcatag gtcactaaac
64981 agtttctagg gacatggaaa aaaaaatgcc atattgcaga aatgcaatat tttgggatga
65041 taaaaggga gtttcaaaaa attgaaaaaa tagcagttac tatgacctct tttggcaaaa
65101 ataattatat gtaatattgt tcatggaaaa atagactgga aatataacga ttaaaatgtt
65161 aattgtatct gggttggtga gattacatat aattattata tataatcttt actttttag
65221 attgttgttc acagtgacat caagatttgt catgggagaa aaaatgaaga agattattat
65281 tttgtagtca cccaaggaga gaagaagtca catctctgga gatagggcga gtagggcat
65341 atgagccaat cacatttctg cagccttttg tggatacaaa aggggtgggc caagcctttc
65401 caatatccct tttcctcctt ggtacccaga cagactatat ttaccagcct cctttgcagc
65461 caggtgtggt catgtgactc attcctggtc aatgaaaggt agatggaagc ctggcctagg
65521 aaacaggtct acatgcaatc ttccattctt ctcccaccca ctggctgaaa agaaaggctt
65581 ctgaggacac agagtggggg gaaggctagg tagaggctgg atgggaagaa agcagggttc
65641 tcttgctcct ctcatcagag agctactgag gagacccacc gcacccagac ccccatactg
65701 gactgttaca ggagtgagaa atAaacttTg tttagaccac tgaaatttga gagttagagc
65761 tattagccta ccctgattaa cgctgtgggta gcccctcaca tctgcccagc accctcagca
65821 gagcctaacc caatcatcca aggttaccca atagagaact caggcttcca ctagagtagc
65881 cgtcacatag agttactggg tcttccaggt tctgccacct ccaccgtgtt ttgtgggact
65941 ctccactgaa ctcacaaagc acatgtattc agctactcca aagctatgtg tactcagaga
66001 gagaaagttc taaatgtttc tgtgaccttg tgccactgat atcatgggtt ctatccttca
66061 gagtgctaag aaaagtgtta aatctccaga atagctttgg aaaagtggag aaatttgaga
66121 ctttctctat ttttagttgc taatatgcat tcctgaaaag tttatttaaa gccacaagga
66181 aatatttcca tattgaattt caatattgca atatactatt ttagaataaa atggaaagat
66241 ccagggacata gaggcagctga gaagctcaac agttggccac tgggcttcac tcagaactgg
66301 cttctctagg ctgcaagtca taagtctttg tgtcacccac tttagaaga catccccctg
66361 acttctggga ccaacctgag gtttgtagga atctctgagg atcaatgatc aaacatatat
66421 tagcttgaaa aaaaactaat atatgtgtat gttttttaa aaggttaagt ttttaacaat
66481 ttagacgtct tggcattata ctctgagaac gttaaccaat gatgaataga gtgacaattt
66541 agatgtaaaa cctcttaaag gtaaagataa aatcctaacc acatggggaa aaccatgtgt
66601 tctgtggatg atttccctgg atttctcaaa agactcttag aatgttctgg gtatgacttt
66661 gggggcatct gttctatgaa gatgggcacc ccagcatcac ctgcatatta acccttcttc
66721 ttgctcctaa agatgcagaa ttagctgaga ttaggaagat gtacaaagtg ttctccctgc
66781 acttcaacta atgaacaaaa ctttttaaaa attacttatg atttggaact attttatcat
66841 tttatRtatc ctatggcaac tggcatttta tatttaattt tatcatcttt tgcttttttt
66901 ctttgatctg aatcaggatg ctaagtttgt gggggggggtc ctacagtttt ggcagagacc
66961 tcattctaaa aaagaggtac cagactatta aggcagaatc tgctgagggt ggccacaaac
67021 ctggtctggt gaacctcact caactcatca ttgatttcaa gggcacagaa gaggcaagga
67081 gatgacagca ggagaaatgg acatgtacca tggagaaagg ggaccaacca caccttctgt
67141 ccaaactgag atttcccagc ctgaaacagg tcaacactgg ggttagcaag aaacttttaa
67201 ctgaatagga gattaaagta ataagaagat gagtactatt attgKtacaa attatattgg
67261 taatagtttt aagtttcatt ctttaagaca gggtgaatca cagtcccttc tctcaaggtc
67321 cttgtcagca ttctactttt ccaaggacat tcaaaaattt ctcatccaaa gtcaaacatt
67381 agtgtgtgtg cctcaaacaa gaaatagttt tccatcagtc tccaaatctt tgaatagtaa
67441 atggcaaaag tatggaaatg caagatggag tggggcttaa tgttgccaca acattcctac
67501 aatactggga tagtcttcct tgggaattac tttctttcct atcacgtatc aataaggaaa
67561 gccaaatgta gaaataaaga aatctccccg attactttaa cacacggagg tgacagtatc
67621 agcgcaaatt gagggaagag taaatgattt cMacaaatga accaaaaaca ctttaaagcc
67681 acatttaaga gaaatggagt cataaaggca atatttgtga gcagataaaa aatcagcaca
67741 gaaaaggtg agaaatacac aatgtctttc atcaaggtgc aaggaaatgt aaaataacat
67801 taaaagtacc aactacataa tttgaatata aagagaacaa tagcaagaaa ggagaggga
67861 agtgatggcg atatggagac acagtctctt ttgcatgcac agggcagaac cggtgcctca
67921 ggctggaggg tgtctgtgag taccccacaa tgaaRgcaaa agagcMccca gcattgaagc
67981 cacagacctt gctccatgaa tcctagctga tgggctggca cagagagatc aggagcagaa
68041 caaggaaatc cataggagga tcctcccaaa gtactttttt ttctggtcca aaaatcctta
68101 aatctgtcag aagcaggagg ttggagtggg agaattgcag agcctggaac acacctgcct
68161 gctgatgacc cattctgagg gggttctttc cacttggcag caatggactt ggtaaaaaaa
68221 ataatagatc cttctccatg gatcccattt ccctttttct ttttttttt ttttttgaga
68281 tggagcccca ggcagaatta aagaccaact ctggqaccca aatttttaga ggacaaaggt
68341 tgatataatg gccagcacga tttagtcatt tagatttcag gtatgacaag ctgatgacag
68401 actttaacaa aatcactgaR agaaatttaa cgtcaacctt aaataacagt agaggcaggt

68461 aatataacaa atagagtcaa aatggtttat ctaaaggtct aagcccaaga aacatccaac
68521 aataaaatta atctaaaaca aatttttaa taatcatttt ttttttcttga gacagagttt
68581 cgctcttgtt gcccaggctg gagtgccatg gcacggtctt ggctcactgc acccctgcc
68641 tcccgggttc aagtgatttc ctgcctcagt ctcctcaagta gctgggatta caggcatgcg
68701 ccacacgccc cagctaattt ttttgtattt ttagtagaga tggggtttca ccatgttggt
68761 caggctggcc tcgaactcct gacctcaggt gatccaccca cctcggtctc ccaaagtgct
68821 gggattatag gcgtgagaca ccacacccgg cctcatcttt tctttaacat tacaatttcc
68881 catcatggtg gcacttgaca gtagtgggac tgtccaacag caaatgaccc catctaagca
68941 ctcaggacag aagccatttt aggtcatgaa aattatacag attttgtgag tgaagggcat
69001 ttagttctga gcagaaagta gtcttgcaaa agggaaattt gcaacaacaa caaaaaagga
69061 caaggagggt gacaatgtca agcaaatgat aaccctgctg gagcttcaga aggaaccagc
69121 tacatccctt tcctgcttct acagatgcta tggcagcccc agaggtgtcc cactaggatc
69181 tcctttcaag aaagaatcta gcatgcatct gaacaacctc cagctgttca cacctcaggc
69241 cctgcctcat cccagacagc cctgagccaa tcactgacac agcagggtac tagtagcctg
69301 tcatttctgc ccaacccggg gcccctccaa aggcaagctc tgctccagac ctccccgttg
69361 ggttggtcaa actatccaaat ctgtcacctgg tctgaggctc tccctgccca gtcttgcttc
69421 atcctcattt tatcctctac aggcacagcc tcctcccctc tccaataaaa cactcacatt
69481 cctaatttcg tctcaacatc tgcttcccag ggaacctaac taacacaata ctcctaaaac
69541 caatacccagc aaaaagtgac tttccaagcc ctcatatgaa gactcatttt ctggaaaata
69601 aaatttaata taattccaat tacccatgac gctatttagc catttcaaag gaaatgagaa
69661 agcttcccaa attgtggtcc tcatggagtg aactgatcat caaatgttgc tgtttacatg
69721 agggcacaca ataattaggg ttgtatgtaa catgctactt tcagattttc aggtaagtct
69781 aaatgctttt aattgatgca agaataataa gtccttcagt tgatttatgt catgcattaa
69841 tatcaatcaa aaggttttct aacacatact ttttaatact ataaaatgtg gggttttttt
69901 taatgtcttt ttttcttat tcagagccac atttcttcac atggtatgtt ttacctaacc
69961 taagggttat gttgttcgtt tgtttttaat ttcaggttg aggaatcaag taacaggtct
70021 ttctaaatcc ttttattgga tatatgttag ttttccatta tcataaaaga ctgaggaaca
70081 ggaacagcag catatttgtt aaatgattca caggtaaaaa tatctctctc ctctttggct
70141 gttttctttc ctgatgtctt tgctcattgc caacattgtc tattttatat ataattcttg
70201 caggacattg tgccctgaag gtgaaRttgg acaggtaagg agatgaccca acaccccttg
70261 tcacacctgc aggctctagg tcacttttgt aacacacaat gaaatgggta aattctacac
70321 aatcctttt ttttttttt caaacaataa cagaaagtaa atatttgaac tgggggcttt
70381 ttcaaacaac acaagtcaga aaaaattgac ttgtttttga ctgttacttt aggcatatat
70441 tttgattaa tgacaattaa atgtaaatat aaagatattt taaacttgag gttttaaaac
70501 aaagaatgca agaatcacct ggttaaagtt agatattttg tcagtctcaa agtcagttgg
70561 ctggataata ccatatcata aaattttata agactaattt gaaggtccat atgaattggt
70621 attattgttc gttttcaat attgatctta gcagtgtatt tacagcatac agcagagtta
70681 atgtttaata caaatcaaca agactttcca gaaaatctac aaagaatcac taactaatag
70741 ccatgctcta gttaaatttg tttacttttt aaagtacatt ctcagaagta acatgtactc
70801 tcaattaagY aaaacacaac cagaattttg gaatttgatc tttaaaataa taaaaaaact
70861 ttctctgcta tttacagcct tggttaaaat cccaacatct ggataccaga atctgagcag
70921 caaaatccac ggagacacat gtgcaatttt atgcctgcaa gctcactatt atttagaacg
70981 aaaccaacgt agtgcatcta cccttgtttc ttgctacaca gaatgtatcc agagtacaaa
71041 ctaatgtaga ttattataaa actcagtgtg tagatattat atatatatac acatgcatac
71101 atacacgcac atatataact aaaacaaaat cttcaaaaat aatacttttt ctttctgtat
71161 gtgatgtgcc ctgatagttt ccacttttact ccatcccatt tccttttgtt aatactggcc
71221 ttgactcact tagacaaatg ggtcatgacc tgtagtttgg aaaacagggc ttttcagcct
71281 ggctttaaag aggctggtcc tcaggccagc agaaccagca gcacctgggg gtagtttgtg
71341 gcggcaaatc tcaaggcctg ccctagacct actgaactag gatctgctct tagcaaggtc
71401 cccaggtgac ttatggatgt attaagtttt gagaagccgt cctcctgcat gcaaaagtac
71461 agaatgagta tctgtgatct gaactacatt taaatcgata atgcacctct taaactgtct
71521 ttgttcaaag aacttctatc ctactgagct caaggagcaa cacagtttct agcaagatag
71581 gtgcaaagaa aaattcactt tcaatttcat caactgcttc aagaggttgc agggactggc
71641 tgacctggta tcccagctcc tgcaggaccg agagtgtggg aggtgggttg agggaggtta
71701 ctgaattgac tgcaatagat ccatgagcat ataaaagtgt gcgtgtttgt tcttattcct
71761 gggagaaaat atatagtatt cacctaattt taaaagagtt tatggttta aaaagttaag
71821 aagagctact aagccatgaa aagacgagga ggaagcttaa atgcacatta ctataccaga
71881 taagaaaatc tgaaaaggct acatagtgta tgattccaac catatgacag tctggaaatg
71941 gcaaaactat ggagatgtaa aaagatcagt ggttgtcagg gcctaggagg tcgggaggga
72001 tgaacagaca cagctcagtg aatttgaggg gcagtgaaac taatctgtat gatattataa
72061 tggtggatcc gtgtcatcac ctgttgtgtcc aaacccacag aacatataac accaagggta
72121 tacggtgttt atattaaagt atcaccctaa tgagaactct ggacttggg tgataatgat
72181 gtgttgatgt aggttcagcc cttgttacac gtcagccacc catgtgggaa aatgttgata
72241 gtggtRgaag ctatgtatgt ataggggcag gaattatatg agaacacttg tggtatatgc

72301 tcaagtctgt tgtgaaccta aaactgctct aaaaaataaa gtctgtaggt atctatgaaa
72361 gcgcagacac atggtccgtg agagcacgtc ctctctgcta taaattggtt gtatggttac
72421 aatcatacct agaaaggaga gaaaataaag agtaagtgaa taccgacatg ttcaattctg
72481 ccccagaata caacaaagtc cctgaatcac tcttgttcta ttgttgccat tgcttattca
72541 attcagtcaa ctcgtatatg tgaagcatgt gctacataca taacgtataa tgcaggatgc
72601 aaaaatgatt atgtgatcac ttcaagtaat ttataatcta gcaaacatat aaaacaggca
72661 cacagataat ccttacatag taaatgcctc ctttttcccc aaaatggcaa ggagacaaat
72721 agcaaggatc cgaggacaga gaggcaaaat tcagaaggcc agaaaggcat ggagcccagaa
72781 atccaattca ctcgcgagta agtatcggg agagagtggt gtacaacgtg acagggacac
72841 ctgttgctcc caattgtaat cttttctgat tggtttatgc ccctttccaa ttactgtgtc
72901 catgctaatt atcaactatt tttattatca accctgcaga ggggactaag agaaaaaaaa
72961 aaactgctgc aaagtgatgc tgtgttcatt ttgcacagaa cccagaaatc ctgatgaagg
73021 aaactgaatt ggatgccaca agccttatct cctgtgaatg ctgaatgact ttgtcggtgg
73081 gttttacgat aagatgtact ttcttttata tctattaaac aagctataca gaatactggt
73141 aaatacacag aagtaaaaag aagaataaaa tagataaaat tttctaagtt aaaagctaag
73201 ggaaaaataa aaagaattat caattgatgt gatcaaagaa aaatgtttat ctcatggggt
73261 gttggaaaag gaacatcata aaaattaata ggtagaataa tcatcaaaaa caatctgcac
73321 aacaaatatK acatagctga ggggaactat cattaaaata taatgtatac aaattgctga
73381 gaaactcact acaccttcta aatcatgtca aaagagttgt ttgcatatga gctgtctgca
73441 ctttctctct ctctctYttt ttttttgttc atattcactg caaggtggct tttgtccacc
73501 catgcaaatc actcatatga aggtcacaat gatgtccagg tggccaaagc ctgtggctaa
73561 tcctcagtcc tcatctcacc gagacagcag tttcttagcc cttctcctac ctccactggc
73621 ttctcttctc agctcctctg tagttccccc tcctctttcc aacctgtatg cattggaggg
73681 gcccaaagct caaccctaat gctcttctgc atcttggtcc ctaggtgatc tcacctagtc
73741 acccagcctc agatagcctt aggcttagga atcacaaata tatctctcac atgacctcta
73801 gactcctatc aacctctcaa catcacaatt tggatatcca acaggcatct ccaactcaac
73861 acagccaaac ccccacttttg actttcctgct cattgcaact gtcccctctt gcagatgttc
73921 cttttagagt aggtggcacc atcatatacc cagttacaaa caaaatcttt aaagtcatcc
73981 ttgactctcc tacactgcat atctaatcca tcagcaaatg ctgtcttttc caccttcaaa
74041 gtagatcccc agtctgatca tttctcacta cctcccctttt cgcctgcctgg tgctggcaa
74101 tggcctccta attggtcttc cctgtttcaa ctcttggtcc ccctctagac tgttccccac
74161 acaacagcca acatggttct tttagaactt caaccaatgt aaattatact tcaagaaagc
74221 tttaaaaaat tcaatcagat cacatctgct atgaaccttc caatggttct cctcccgcag
74281 tgtgccaaat aaaatggaaa tgcccttatc cttgcttaac agaagtctac aacacagcct
74341 caccagcatg cctccaactc acatcctgca gctttaacct cactccacRc cagccccccag
74401 tctccttgcc gttacttgaa agtgccagga gagctcctgc caaagggcct ttgcacatgc
74461 tgttcccctct ctctgcaata ctcttccccg tgtgatcata cggctcatgc tcccactccc
74521 ttcgggtctc agcttgaatg tcacctcctc cctatgacct tccctaacct ttcgtgtaaa
74581 attctacctc tcccttcctc agtctcttgc ttctcctgct ttgttctgga gaatacctNaM
74641 cagcaccacc tgatttgtaa ctattccctt gagcacattc tatctcagcc acgggaatgg
74701 aagcttcatg caggcgggga catcatctgt tcagttcatg ctgtagccca gcaattctga
74761 atgattagat tgaaattgga tccaaaaata tcacaaatga gataacgtaa cttgttgata
74821 agtgtgtgaa gagtatgaag agatgatcaa gctcacaagt ttccaagtgc taacatctat
74881 aaaactccat tgtcacccat caaatcagca aagattaaaa accacaatag aatgtgataa
74941 aatagtgctc tcagatactt cctggagaag tatagatggg cagaattggg tgatctggta
75001 tcaatgatca ttctttcata ccaatacacc atgggatttt gcgatcagaa ggtaaagaag
75061 acacgagaag aaaagaaggt gaagattaaa ccagcaaaaa cccataataa gtaggacttc
75121 ttcctattca ttagtaagaa agagttgggt gtccccatgg gaaaatgcta atttagtgtc
75181 ctgaaccact gtacctcca attcctgctt ccccccacaac agtggcccca cactgagtcc
75241 tacaacgagg ataatgatcc tcaaccccca attgcacaga cagggctaag tcagagacag
75301 tgatgccaac cttgctgatg tctctaaaac actcaactac tgggggctaa ccctaagMaa
75361 aattattgac tccgattcct aagttaattt cctataaggt ggaagaagca acaagtgtca
75421 cttctcttct gggctctatg acaccaaata gtggagccga agagacttgc tgatgttttg
75481 aaacccaagg ccaaataatg ctctctaaac ccttagaggt gtgactagga tattcacaga
75541 agccacgcaa aagacagcag ccttcaatga agaaacaaag aaacaaaaaa catggttcct
75601 tttataaata tttatcgatt atctaaggct aggttaattg ttgataacta tcaattatct
75661 gagcaagata cgcagaaaca cttcaggtgc ttgaactgca gcatcctggg ctccaaccca
75721 aacttactgg agaagaagct ttagatacca ggaatctgca ttttaaccaa ctcctcaggg
75781 aaactgcccc agaggggctc taggctaacc atgcgcaact tccacccatt ctcctgggaa
75841 gtgattgtga atctcctcca aacccctctt acacttcctg attaagttgg tgcccctcac
75901 tgaatgtcag cctcactgaa tcttaacgag gaatcgccag actgggggtg gNattgtgca
75961 gcatgtctgg ggaacacttc actacttcac taaaccctgc tgcacacatg ctgaacaccg
76021 ttccaaaggc tacaggaact gagcaccgca ttggaatctg gccctggagg gtgcccagca
76081 tggcgaccct gaggggtRca ggaacccagt gagaaggaga aacagaaggt acagtccagc

76141 tcgagaccac gcacataaag aaatctgtag gcagggtctc tattattgtg ccatattaaa
76201 tatcttgata ttttaaagca atattatttt tctgattata aaagtactca ttgtagaaat
76261 tttaattgtg ccatcatcct gcagaaaaat gaaagtacaa aaaacgaaaa agcagctata
76321 cacggccaca aagtcacagg gctcatcggg atgtgctaac caggctggaa actgatcaaa
76381 gctgatttat tgagaaaaaa taggcagcat atcaaagact tacatcagct tcatagtaga
76441 cagactttgg gggcgggga actctgtctc ttttgagtat attctcaaaa ggataaactt
76501 tcacctttct gtgaagcaca gttactataa atcagatttg caaactgtga gaaatgctta
76561 caactcaatg agtcttttgt cagccagtgg gggctccatc gtgaaatcca cccttcgcca
76621 tagcgatggg ataaatcatc accagccccg agacatcgcc taatccctic ctcgcaaggc
76681 agattcgggc gctttctgca tctgcttcgt gttattgaaa agagctcggc tcatctgctg
76741 ggctctcagg cttcacagtg acctcgcaca gaacgctgct acttctgaaa ctgttttaga
76801 ctcttccgtc tatgaaacag acacagagtt taagtttagc gtctttatg gtcagaaata
76861 tttagcgtta cttccagagc ggcagccgtg gaacaatgtg ggaaagaagt gcttcagttc
76921 actttctggg aagtactgac cctgggtcaa tttaatttit tccgtaagat ttcccctct
76981 tacttttctc cttccactgc tatatgtaac agtatctccc cttccactgc tatatgtaac
77041 agtatctccc cttccactgc tatatgcacc agtatgctag tatacaacat tatagattaa
77101 taatatgcta tattgtttaa aaatattaat gttatataat taacatggtg tgcatattat
77161 tatattgaca atacgtaatg tgatgtgata ataagtctca ctgagtgcca ggcaccgctt
77221 tgaatgctct aaactcatta gctaatttat tcctcgtgat tctatggggt agatgcacta
77281 tttcattccc attttacagc tgaggaaact gagggcagcta gtaacaggtg gagccaagct
77341 tcacactgag atcatctggc cccagcacac tcataaaaat gagcaaaagt ataaaagcca
77401 aagggaaaag gaagccaagg ggtgaaaatc ctaattacaa acaaatcctg ggtaagctgg
77461 gtttttagtc cttccccaca tgtgaacagc aactagaaac ctgaacagtg actttgtttc
77521 ccctgtcatc cattgttggt gcctgatcct cacacaaaat cttacggagc agtatctagt
77581 gattagctta gctgaattga gcctggacac ccttcatgag ctggaggaca gaggacgtgt
77641 cgatggaggg tccaacttca ggcatctgta ctcgcctgct acaggtgagt ggacctatga
77701 accccagccc tcatcaagca cccgagggtc acctgcctgc ttcacctgga agagacagca
77761 aggtgtgatc ccaggaagat cctctggcag gaggcttaca gccgagagca gcggctgctg
77821 aacatagatg ctgtcRgcag gacacagggg tgataggggg tgagccagtg gagcaggtga
77881 aggtgcagac tacaggcagc ccccctgaga tcctgcccag accccagcag cagctcccct
77941 gtccctctct agcagcttcg ctgtgcccga agtgtttgag aacaggtgac ccatgccctg
78001 agtggcagat gctgtgtctt tttgatccct tctctccctc ccccccacc cccagtgggg
78061 tacatggaag gtttgctaaa tgtttgttga atgaataaac gagcccaagt cagaagcagt
78121 ctccaaatca ttcctcatcg caaaagggtg cggtggaaaa actcacaaag ccaaggcagg
78181 aggacacact caacttggaa acggcccgtg cccagctttg gaacaggcac agcctgagct
78241 tcaaggaagt cacttgacca gcagtagctc ccactttcc ttgcagctag aacagcatca
78301 gaccaagtga tctctaatgt gatgatttgc taaagtacaa tgagttttac aactagaaag
78361 taccttcctc tcaagactga cttcactatg agccacctaa ttttcctcti ctcttcttct
78421 ggtatttttg ttgcaaatag tacacacaMa acaggatata taatctattt gtgcaattta
78481 aagaataaga agcaaacacc tttgcaKgta ctccctagtc cacaacagtc agccccagga
78541 cctcagaagc cccttatgcc tttcccctaa aactctcccc tccctgacaa ggtaattcca
78601 atgctgagtt atgtggtttt ttttccttat ttttcttttc aacacatatt acgtttctct
78661 gaataatatg ctttttaatg ttgcctcttt ttaatcttta tttgtggaat catattgtat
78721 gtaatctgtg actttttct actcacatat gagaaccatc cacactgata catggctaca
78781 gatagacact tggagtttat ttttcactgc tgtatagtac tccattggtg gagtacaata
78841 ggtttatgta tccactttte tgtagatgga cacttgggtt gttctgtttt tgctcatcaa
78901 tacctcctgg tgctcaggta caagggaata cagacccagg gtgagactgc tgagtcacag
78961 gctaggcaca tcttcagctt tactaggtaa caccaagcca atacaaaagt gcttgtacaa
79021 actcatgctc ctgccagcat ggaggaccca ctgtgccaca taaaaacatc actgttatta
79081 acttgttttа tttgcatatg attatttttt cccttatccc caaccacttc tcaaagcaac
79141 tagccagcat gtgccacaca ggcaagcacc cactccaatg tgatctatat ggttaggtat
79201 gtatgtaccc tggaaaaccc tgtgatgttg cttgaggagt atataacttt tttatgtatg
79261 taagtagcat gtgctacaaa gcgcgttctg ttttctgtat ttttcactcc actcagtgtt
79321 ttgtaaaaca tgctcatgtt gctccatagg tatcagagac aggatgatgt tttatcttta
79381 agatgggtac gccaccctca ttttatagat cacagtgata gctccacaatt gtttagtact
79441 cagtggggtc taaatgtact aactcgttta atctcccacg aaccctgcaa aacagatgct
79501 tccgtttcat ataaaatgag accaaggcac aaagaaacta aggaacttgt acaaaatcac
79561 caagttagta aacatcagag caggatttga attgagccag aatgtgttct tatccacgac
79621 atgaaactgg ataagaatgc aaagctcaga gaatttтcat gactagcatc tctgggattc
79681 acagctggcg accacggagc agaactaata tacagatggt tcccctctca gtccagtcct
79741 cattccatcg gctccaaaat gtgtattatt ctatatgatt agctggtgaa caacaaaggc
79801 aattagttag tcctcttcag caaatgttag taaatgaaaa tattatagag acagaacttt
79861 ttttaggaaa tgcaatcatg tgaatttaaa aatgctttat cagaaatага attaatgaca
79921 aaaatattta taggatccta agaaaatgga tttgctattt tttttgtcgg ctgatgataa

79981 tcatctgggt gcatctttgg ttgtgacagc tccacccctt cagagagttg Katcttcata
80041 cacacctaac atgctaagag tagatgtgca tgatatggta gttagtataa tttctgtaat
80101 aaaaaaagta cttggtcatg cctgtaatcc cagcattttg ggaggctgag gtgggaggat
80161 tgcttgagcc cagagtttga gaccagcctg ggcaagatag tgagaccttg tctctacaaa
80221 aaaaataaaa attagctggg tgtagcggtg cacacctgta gtcccagcta ctcaggaggt
80281 tgaggcagga agatcgcttg agcctgggag gcagaggctg cagtgagcca taatcatacc
80341 actgcactcc agcctgggca acagagcaag actatgtctt aaaaaaaata aataaaaata
80401 aataataaat aaaaaatttt taaaaaaggt acctggaacg gcctgcaaag aaagggaaat
80461 caaattatgc ttcaagacag tcactattat cactgacaga gaagcagcta aaataaacag
80521 cctgctcatt ttgtttgtaa atgaattgcc acaattcttg cactatttaa atcaagaata
80581 ttttatattc catagttttc aaccacccct ccttttttta ttgtttccag ctccttaaac
80641 atataaaagg ataaaagcca tttgttctgg cagaaaagag tcatcataaa ttttgcagag
80701 tgaatttctc taagatgaaa ggaatgttcc tctcctccag gacagcctac ggacaggact
80761 gtgatgacac agagtcttca cgggaatcac acctgcagtg ttaagccact tctgtggaaa
80821 actcaagtcc ttctcagata acaaaaacat tttagtagca atgaaccaaa aacaaaatct
80881 tccactatat atgttaatac atcaaaagga accattcatg tgccatttat aagaacttcc
80941 ttccggccag gtgcggtggc tcacgcctgt aatcccagca ctttgggagg ccaaggcagg
81001 tggatcacga ggtcaggaga ttgagaccat cctggctaac acggtgaaac cccgtctcta
81061 ctaaaaaaaa aaaaaaaaat gcaaaaaatt agccaggcgt ggtggcaggt gcctgtagtc
81121 ccagctactc aggaggctga ggcaggagaa tggcgggaac ccaggaggca gaggttgcag
81181 caagccaaga tcgcgccact gcactccagc ctgggcaaca aagcgagact ccatcaaaaa
81241 aaaaaaaaaa aaaaaagaac ttccttccca gaaatcatag cagcgttcct cagcccaaag
81301 ccagaagaaa cttctcgcac atgaaatttt acttcaaaaa ctcccatatc aggcatttta
81361 atgaatcagt ggaagaaaat tatcctccca actttgttgt caagaacccc aatttcatat
81421 gcagaaaaaa gaattacaaa aataattatt cgaattctaa ttggtgggat tttgataggt
81481 ttataaagga aataaatatc tttaacacaa ttctacctcg cagccaacat cagctattag
81541 caaccacact tcttattgcc agttcatctc tccaaacaca cagaagccat gtgagttgaa
81601 atttattttt taaaaactct cagttatgat ttctcaaaat tatatttcat atattgacat
81661 caaccaatat gatgatgata ttatatattg acatYaacca atacgatcaa ccaatatgat
81721 gataattgta gggaaaagaa agagagatct gactgttact gtgtctatgt agaaaggaaa
81781 gacataagag actccatttt gaaaaagacc tgtactttaa acaattgctt tgctgagatg
81841 ttgttaattt gtagctttgc cccaaccact ttgccctagc cactttgacc caacctggag
81901 ctcacaaaaa catgtgttgt ataaaatcaa tgtgtaaggg atctagggct gtgcaggacg
81961 tgccttgtta acatgtttac aagcagtata cttggtaaaa gtcatcgcca ttctctagcc
82021 tcaataaacc aggggcacaa tgcactgcgg aaagccgcag ggacctctgc ccttgaaagc
82081 ggggtattgt ccaaggtttc tcccatgtga tagtctgaaa tatggcctcg tgggatgaga
82141 aagacctgac tgtcccccag cccgacaccc gtaaagggtc tgtgctgagg tggattagta
82201 aaagaggaaa gcctcttgca gttgagatag aggaaggcca ctgtctcctg tctgcccctg
82261 ggaactgaat gtctcagtat aaaacccaat tgtacatttg ttcaattctg agatgagaga
82321 aaaaccgccc tatggtggaa ggtgagacat gtttacagca atgctgcttt gttattcttt
82381 actccgctga gatgtttggg tggagagaaa catacatctg gcctatgtgc acatccaggc
82441 atagtacctt cccttgaact taattatgac atagattctt ttgctcacat gtttttttgct
82501 gaccttctcc ttattatcac cctgctctcc tactacattc ctttttgcta aaataatgaa
82561 aataataatc aattaaaact gagggaactc agaggccggt gccggtgcag gtccttggta
82621 tgctgagcgc cggtcccctg agcccactgt tgtttctcta tactttgtct ctgtgtctta
82681 tttctttcct cagtctctcg tcccacctga ctagaaatac ccacagttgt ggaggggaag
82741 gtcacccctt cagataataa gataaatcag agccRaaaac atagttcatt cctgRaatca
82801 aatatagaac gtttctacca acacacattt tcaaagatgg tgttttcagg tttgtatggg
82861 attgtttcac ctttatgaat tagcttttta aaacctgtaa tactttcttg ctgacttcat
82921 catttccttc tggttgcctg gaggggtggt gtggaatgct aataaaatga atttcagttg
82981 ccgtccctca caatctgaac tatagaagat atttattgtc tcaacttccc tatgagcttt
83041 tctttgcatc atgcagcttc atggtcagca gacactaaaa attaaagaaa gtctttctcc
83101 cactttactt gtgtagcaca gacacactga tcaaatatgt tcccagcact tccgaagaaa
83161 ccttatcaca tccacaagag atttcctact tgcacttttt ttgataaaca caaccatcat
83221 agcccaacaa aacatcacac agaaatcaaa ttatagtgtc cccataagca tctgctcctc
83281 tatggccttg ggcaaaattt agaatcctcg acatccctag agttaccaca atctctgaaa
83341 gtgaaggagc acccacaaag ctcaaggaat gcattgaaac tcttattact tccaattcca
83401 ttttcaaaaa aagtaaatgt gtgtgtatgt gagctgcaca tggtccagaa tgcctcacca
83461 aatgtattgt tttaaaatgt gtgtacgtcc atgtgtaatt gtatgtgtgg gattttgaaa
83521 ggctttttat attttattca aaaaggtaca cttttcaata tcacaaactt tgctttcaat
83581 tataagccct tcccatttc aattaatgtt ttaggcaagg aatatacatt agtaaaacca
83641 accacaccac ttagggaaaa tgaattagta tggggaaagt gaagaactgg ccatgcagtc
83701 aattactttg gccagcatag atatagttga actaaccagc acaggtgtag acagcctgtt
83761 tggataaggt agcttaagcc ccaatttttt ctgcagtctt tattttgtc aaatatatga

83821 aaactaccat ctcatttcct ccctgtagct attacccaca tgtatgtgta gtgtcaaaat
83881 aaatggccag agtcctctca gggacctccc ttggcacaag tcgcacttcc tcacctctc
83941 acctccagag cctcaggaag tgcaggtcag aaagcagcca gggcaggtgt gaggtgatgg
84001 agcgctgagt gtcggcgagc ccagataaaa caacgttcca acatcggaaa tccaatcatt
84061 cacctacttg ctcctgctc gctaacccca ggcaagtata aaggagatgg aattataaca
84121 ggagttagaa gaatttggat gtgatttcat atattaactc agcaaaattt tttctgaaaa
84181 ggtccagaca gtaaatattt tcagctggca ggccatatgg tctttgtcga acctactcaa
84241 ctgtgccatt atggagtgaa ggcagccaca gatgatatag aaatgaatgc atggggctgt
84301 gttccaataa agctttcttt atggacactg aaatgtaaat ttcatgcaat ttacatgtgt
84361 tacgaaatat gctttctttg atttttcaac catttaaaaa agtaaaaacc attttcttag
84421 ctcctgggct gtgttgactg acccctaatt aactgatatg tgggctgcta tccatgaaaa
84481 cctaggcaca gaggaaggca gagctggctt cccagccaag acgggactta ccttgatatg
84541 agctgctggg tccgggacag tctgaatcat gtccttcagt aagccagccc atctaccagc
84601 tgttcagaac Ntgacggcta gaagacaaaa ggaacaacat acataataat aaacaaYtgc
84661 atttcgtgt tttatgttct agcaggacag gaMacaattc accaatggca aaagaatcat
84721 agctcttacat taaacatgtt tgcctaaagg catcctctag gtacgtgtgg tccatgaggt
84781 gactagataa ctcacttccc ttccattggg aaaatcactt acaatgagcc caagagaacc
84841 ctagtccgac aggacagaag aatctagctc aagctaaccc acatcacatg cagcatccac
84901 acatccttcc acgtgggcag catctaatga gggatccatt aaaggaagac gtgggactaa
84961 aacagggcat acttctctat catactgaga aaacaggact ttgaaatccc accaaaactN
85021 atgcgatctg cacatccttt tcagcttYgt tattaagttc ttagtaaaca gcacagctac
85081 cattcattga gtacttcagY gccagttcct tgagcgctaa gggctccaca cacattttct
85141 catttcattc caaccacgac tctgagagct gtcattccca tctgcagct gtggacgtca
85201 agactcataa aggttactga tttgtccagg atcacctggt taataagcga cagaaccaaa
85261 cttcaaatca gattaggcta tctgactcca gagcccaaaa aaaatttggt ttgacttaat
85321 tagcMggtat caacccacat tttgaaggga catttttaaaa caccgcttaa ataaattaaa
85381 tttaaagatg cctataatcc aggaattttc cagaaataaa tacttcatcc aatatattcc
85441 tttattcaaa tYataaagca gcatgttctg accactgtct gtgccctccc cttcaccgga
85501 gccagtctcc aacctccctt tgctgtcaca ggccccaggg ctgacctcta cagatgggct
85561 cagcaggtg ccttgccttc tggccacctg tcagggttgg ttgacgtggc ccctctggga
85621 gagcaggggt gagaggagag gggtatctct tcccctcacc ttcccaccac cgacacctgc
85681 cgcccaacct ccctgggcgc ttggttatgg ttctgactgc agctggattc tagggggacc
85741 tctcccgtca tggggcccct ccttccaggc tccagcctcc agtacctggt ccccagccag
85801 tctctggtgc tctgcagatc tcagccaagc catcagttct cttttggcac taaaaatgcc
85861 tttttaRtt tacatttta gaagccatca cttgcttttt atcacctgta gtttttgtt
85921 tgtttctctc tttacRatgg ctctttgcag taacaaatgc aaaataaaaa taaacaatat
85981 gattacagaW cttgagacat tttcgaaggc tgtctttcaa atttgctact gagcgcatta
86041 ctgtagtgac aagtgaaagc attcacagga gtcctcccca cattcacatc tgtcctttct
86101 gacctctcac ggtacaggca cacccattcc aacccaatYg cctctcatga agagcatcta
86161 cctccagatc tgcatgctcc acatctgtct tcagtctccc tggaggcctc ccaagattgg
86221 cggagcttgg ctcaccaaga agatgacatg ctgggaacct taggcatttt ttttctataa
86281 ccaaatttct aggtcttgga aaatatgtac ttccccccac ccccaccccc aggcctaaag
86341 tccctctggg ggatgagagt tactgaaagt acagagggag tgaagtgcag tcctgaaatt
86401 gaaccgggaa gcagatgaag gtgaccaggc tcctggtgct ctcgtgggag aagaggctgg
86461 gagaggatgg ggcctggctg aaggtttctg ggagcaYagg aatcctcaac tccccttatc
86521 ctaagagcag caggtgccac aggaaaacac cactctgctc ctggggtcat tcagcccgga
86581 aggggagcgt ctgcaagcca tcctcacaaa gggagggcgt cccactgcac aaccctgctc
86641 tggggagcac atggctattt ccgtatgtct ggacattctc tctggactag ttcactccgc
86701 acagttcctc cctgcctgca cacacatgct gacgctcaca ccagggactg aagctcgtcc
86761 ccctccctcc aaacccaggc tgacctgtgg ctgcctctga cctgcagaac acagccgagg
86821 gaaggtttca ggagtcccag gctcaggcct ttatggaagt gggagcttcc ccttcctgcc
86881 tcctgaaacc aagtccccat accctcagca gcacagcaca tggcagagga ccgagtgccc
86941 agtggggcag ccagcaccaa cgccaggccc gggagggagt tgtcctggac agtccagaga
87001 actgactctc agatgaccac ggcccctgcc gacatcaggg aggcagcttc cagctgagtc
87061 cagtcagccc acagaatcat gaccaataat aaatgggttg ttgtactaag ctgctaggat
87121 ttggggtagt ttattacaca cacaggtcat tgaaacaccc ttgtaagtgct ctagaggcac
87181 ggagaagata gagggtaaat agcttgtttc actgtcacta tggataagta caaagRtggt
87241 tccaacaYtc aactcctcct gtacccatgc tttttgccac ataacttttgt gattcttccc
87301 attaaagagg tagaattact tcccaacctt tatttttggg cggcctatat gatctgcttc
87361 agccaacagg cagtagcaga aagacaagta tgacagatcc tagctgaagc ctcaggaggc
87421 aggacatgtt ccccttttgct tttctgtaac tttccaccag catgggaaca tggccagatg
87481 catgcgggag gatgagaggt acctgaggca gagtcaccca ccccaatcac ccSaccaaga
87541 ctacgtttga tcatcccata gacaaccaaa accccagaca tgggagggag gcaaccagac
87601 cagccgctag ccaagtccaa ccagaatggc caacccacag gctcatggct gaataagtgc

87661 ttactgcttg aagccactga aatttgggga atttgttaca cagcattttt gtgacaatag
87721 attactgaca tacactttgc aatgtacaat cagattaccg agatcttcgt taaaattttt
87781 ctagccagtg ataaaaggag actcaaacag ggcatttcaa aggaagccac ttcatctcaa
87841 cacagagaca taatatttcc actcacctac gagacatgat ctcaaacccc aatcctgccc
87901 tcaaaatggg tYtggaaact gaaggataac caagaaacct ccaccagaag cctccatggg
87961 attcccagag cccttcccag gagcaactga attctcactt cacatgatgc cctgccagcc
88021 tcccctggat tccaaaaatc aaaacatcct tggatatcca agaccgcagc aacatcatag
88081 aagttacagc agccactcgg tctgtaaMca accaagacat aaactaaatg agcaactgtt
88141 tgagtctctt gtttcttatg gggaagtttt gagtactcag gttgcatcaa gtataaaatg
88201 acagggaagg gaatagatag agattccaga tgcaacacag tcctgatcct tgagggatcg
88261 agatgggaaa cagatctgtt tcatacagat atgaagcggt cagtcctgag agcaggcagt
88321 tagtggaggt gcccagtgag gcgtgtggat atacctagag gaaagagaga gctgattcat
88381 gcagagacaa gagggtgcca ccaaggagcc ttgatgaaca agaagcatga ggactggagg
88441 aaagagggtg aaaggcatga agcagggaac ctaagtttct cccagctctg ccaMattaga
88501 gaccaaggcc gtatgagctt ctcacaccgc cacaccacga gtgatcacac accaaaggga
88561 ttcactcagc acgcagcgtg atggcactgc caccctccac accagctcag cgaaaaccca
88621 acggacctaa agaccaggag aataaaagct caaccacact cccctgcctc ctcaacccac
88681 acggatctct gactcttttt ttttttttga gacggagtct ctctctgttg cccaggctgg
88741 agtgcagtgg tacgatctcg gctcactgca acctctgcct cccgggttca caccattctc
88801 ctgcctcagc ctcccaagta gctgggacta cagccgccca ccaccacgcc tggctaattt
88861 tttgtatttt tagtagagac gggatttcac cgtgttagcc aggatggtat cgatctcctg
88921 acctcttgat ccacccgcct cggcctccca aagcactggg attacaggcg tgagccacca
88981 cgcccggcta atttttgta tttttagtag agacggggtt tcaccgtgtc ggccagatgg
89041 tctcgatctc ctgacctcgt gatccaccca cgttggcctc ccaaagtgct gggattacag
89101 gcgtgagcca ccacacctgg ccctcttga ctcttttttgc agccatttga gtgcctgttc
89161 tttttacca tttcagaggt attttctgga ttttttaaag agtacttcta atttacttct
89221 gtgttcctaa tggtcatttc tcaaatatgt agtagttggt aaccaaacaa actaaaacca
89281 tactaaaaat ttttagtagt tggtgatagt ttcatgtcac tgtaggaacc tttttatttt
89341 ctattttacc tgccttttgaa cccttgcaga acttcactct atgttgattg aaaatcattt
89401 ctttaatact tgtttcttgc aataaactca tttgctaagg tatatacttc catatgattt
89461 tgtgtttcat gacccagcta tattttatta ttgggtatct taaagaaaca aaaaaggcct
89521 taacaataac agaattctac ttgtgtcact tctttgtttt tgttttcaaa atgccaatgt
89581 cttactaaat agaaacaMac ttgatttgaa ttacgtaagc tctaaccaca taaaaaagat
89641 ggactggtac ccaaggtaga agggaaaata agcattttgt aattatggag gcagtattgc
89701 aaaatggtta agagaaggcc taaatatttg cagggctggt gcaagaaaat agatggaagt
89761 ttgagacccc tcgaccctac ccctcctctc ttctcaaacc caattgtgtt ctgcgggtta
89821 ggggatgcat atagtcacgt ggacatccog atccacatgg ccacactcca ttcagcaatg
89881 ctccctgctc atctttcaga cccagggaaa cacacacaag atcttcccaa gaagatgaac
89941 tccaggaaac aggctggtgc agcccaaaag atgctcagtc aagtttggaa aggcactctg
90001 ggtgccccag cacctggggc atgtcctgga atggggatgg gttcagctgg ggagggcagg
90061 aatgggggcct agaaggcata ggcaggacgc tgggctgggg gcagtgctcg atatgagcac
90121 agtgcagagc cagatgaggg atggaaatca gatctgccac ttactccttg gaaacctata
90181 aatgatcact ttatcctcca agagccttag ttacacattt gcacaatgag gataWtatta
90241 ctgtagtata ataagaactc catttgccct tgtctctcgt ttctggcatg gagctcctaa
90301 aactctggga atttcccaag tgatgggagc atcttttgtt ctaagaaggc agcaggttgg
90361 tgagtcccta gatagcttca ggatgggggc taattgcaag aaagagtgag tcttgattag
90421 atgctcagaa ccttcagccc catttcccaa cctctcagga gaggagagga gctagaaatt
90481 gagttgatcc ccagtggcca gtgatttaat caatcctgcc tatgtaacaa aatctccata
90541 aaatacccctg acggggttag gacagcttct gggctggtga gcatattggt atgaagagtg
90601 tggtgcaacc caatgctaaa gggacagagg cggccaggcg cggtggctca cgcctgtaat
90661 cccagcacct tgggaggccg aggagggtgg atcacgaggt caggagatcg agaccatcct
90721 ggttaacacg gtgaaacccc atctctactg aaaatacaaa agattagccg ggcgtggtgg
90781 tggacgcctg tagtcccagc tgctcaggag gctgaggcag gagaatggcg tgaacccggg
90841 aggaggaggt tgcagtgagc cgagatcgtg ccactgcact ccagcctggg caacagagcg
90901 agactccatc tcacaaaaaa aaaaaaaaaa aaaaagggc agaggctcct gtacttggaa
90961 tccttccaga ccttgccctg tgcacctctt catctggttg ttcattcata tgcttaataa
91021 taaactgtaa tcataagagc atagcgtttt cctgagttct agcaagttgt tgcacctaaa
91081 aggggggttg tgggaacccc caatgttgta gccatgtcag acgagtgtga ggtaacctgg
91141 ggacccaata cttgtaactg gcatctgaag tgaggacggt gttgggagc tcagccctta
91201 aacccatgtg ctaacttccg gtagtcagtg tgcagactga attgaactgt tgagcaccca
91261 gttggtatca gtgttgaatg actggtKggt actggcgaag acatgatgta tttggtgttg
91321 ggaaacatga ataaaaaatt tgtaaaacct ccaaacgaYg ttcagcaatt cacaaaggtg
91381 tcagtgcaag agttggcctg tatctattct aactggtcag tatgcaagtt gaaccattgt
91441 ttgattatct cctctgtcta caccatcagg cttttgtgag gattaaacta aattatgcct

91501 cagaaagaaa actctctcaa ggctaggcac ataatcaaca ctaaacaagt ggtaatcatt
91561 ataattaaqa aagtaaaaat atttcaaatg gacgattttg atactgtata aaatgttgca
91621 actttttttt ttttgagacg gagtcttgct ctgtcgccca ggctggagcg cagtggcgca
91681 atcttggctc actgcaacct ccacctcccg ggttccactg attctcctgc ctcagcctcc
91741 cgagcagctg ggattacagg cacgtgctac catggctggc taatttaaaat gttgcaactt
91801 tttaggaaaa ataatcctca ataaataaat tgctaatttt cataagagcc ctttgtcaac
91861 tgactaaaaa catcctttaat ttagaaatgt atttttagt tttaagataa ctagtcatta
91921 agtgaaaaca ttgtaggcaa aatggctcta agcaatttag tattcatagg aatgaatcca
91981 ttccttgaaa gcattggtcg ctgggtgcac ttgtcctgga tgagcagata ttaggcaaat
92041 cagtctttca ccagcaaacc ctgccataag aactgcacag gcctgattcc tgccaagcac
92101 accaggcccc tgactggggc agaggcctcc cttatggggc aggaagaagg aggcagggag
92161 aaacataggg cccatgattt aaggaggctc tccctctcag gctcatgcaa gtgcaggatc
92221 agtacctaaa ggggagcacc gcccgaaatc ctgtgcccca gtcaccttaa cccagtccag
92281 ccctggctcc tgcactccaa agctaagcag ggaataccag cgggagacag aagacagcat
92341 gagaaactga atgcatctcc cacatttatc taaaaataag aaaMtggact tcttcagtag
92401 gaaatggctY atctttccaa atgaatаaaa atacttatag ctatgggttg aattgtatca
92461 attctctccc ccagttcatg caatggagta ctaaccccag gtccctcggg atggtgatgat
92521 agagaggtag ggcctttaca gaggcaatca aattaaagtg aggtcattag tgacctaacc
92581 caatgtgact gatccactta caaaaaaagg gacaagattt aaagacagac ctgtatagaa
92641 ggacgatggt gtgaagacac agggaaaaga caaaagaggc ctggaacaga ttttcctcaa
92701 agccctcaga gggaaccact tgggctgaca ccttgatctt ggacatccag cctccggaac
92761 ggtgagatga tgaatttctg ttgttttaag ctacccagtt catggcagtt tgttacaaca
92821 gcactgggaa aggaaatcac ctctatggag ggacttacga aagtcactta actaatgcag
92881 attagaggcc tcacagtcaR ggcatggcct caagagccac atccatttta attgtaccat
92941 ttctcactga actctgaccc tggtcaaggc atgtctcagg ctccatggac tactattcct
93001 tccactgatc gaccctggct tcattctggc aagggaggga ctcatacatt ctgcggcctg
93061 catgagtgtc atgtgagcac ccccataacc ttgatcctg cggtgcttct ccagggggagc
93121 cctagcattc cagctggcct catggcatg cctagagacg agggagctga ccctctcctt
93181 cttcaactgg atttatttt tatttttttgg catgttttgt gaatacaaag attcactgcc
93241 tggtgtgcc ccttgaaaga agtttтcaat tgcattcagg tgaaataacc acaaaatgac
93301 tgtaagccaa atgtagtagt atgatagaaa aatggaaata tcgtaaaagc accagtctgt
93361 agacacctag cttctggttc ctctggaaaa gggagaagag agtagacagt gatggagaaa
93421 agagggggctg tgaagactat agaactgaga aggcagtaat tctaaaatct ccacactgta
93481 gggccaggaa caggcagtgc tgggcaatgg ggcatcttat ctcagggaag tcaagggtgt
93541 catgtagaac caacataatt catccaagta cagcaaagaa tccagaaatg gtctgtggag
93601 gtttggaacc atgaaaatca aatаggaaag atacaaaata ttacatatcc cacatttttt
93661 aaaaggggtc ctgactaggc agcataagat tatttgggtt ctgttcattt tacctttagt
93721 tgcccctggt tctgccatct ttttcctctg tgagtcattt gtcttgcttt tggtcaacac
93781 ggcttctccc gggctccaaa agatcctgga atacctgaa tataagtgga agaatatcaa
93841 accttatttt gttttcaaat attaatacca gggatcaact gtacatgtac cgacaaaacc
93901 tatttcttaa acattatttt aaaatatcct aaaaggggaa agaacttaaa tccttcccct
93961 taaaaaaaga ggggacaaca ttcctctcct ctgagggaag cccagcatta tgaagcaaaa
94021 atcgggagtg aaagcaaggc caagcctaac tggcatgctg aagcacacag atgcttttgc
94081 acagaaaata ttttgaaaat gttttctttt ccttatagcc cccagctttg gtaataatgg
94141 cttccctaga tcattctgtt agcactttct gctgctcaga acagggtagt gggattaga
94201 atttagaaaa catcccgaga actgtaatta agcaattgtc atagtcccag aaaagaaaca
94261 acccttttac tttgtaaatg ctaggaggat ctgtattttt taaaatctta gaacactaac
94321 tagctaaaaa gatagaaaga aaaaaatctt tcttacaata tgcctgtagc acggctccaa
94381 aatccagtcc ctctctctct tctttttttt tttttttttt tttttttag atacaaggaat
94441 ttctctacaca actttccagg taaaatattc aatccccaaa taatatattt agtaRaatcc
94501 ttacaacatg aRaaattgta aatggcatct gtttccgttg aaaatatttt taaattagaa
94561 aacatcttaa gcactgcatc aaatcaatat ttgtaatggg cagaattatt tctaaatggt
94621 tccacaggcc agttgacatt cccactctac ttaggaagcc cccagccaac tccacctgaa
94681 gtcttcgaaa cctatgcata gaggcaaatt gcccagatgt cacagaaaag catttgttgt
94741 gatacagaaa atаaaacaca ttactggggg aaaaaaatca gggtactaaa ccacgtacat
94801 aatatcatcc caatattgca caaagaaaaa aaaataagtg gatgaaataa aagaggggaag
94861 gcaggaaagg aaagaggatg acctgagaaa agttatcaaa atggttaaca gtcatggtct
94921 ttggctttcc agtgtgaaat aggagttctt attttcctct ttttaaaata tttttaaaat
94981 tatttatttt ttaaaccaac taataaaagt aatatatatt taccgtgtac aacattatgt
95041 tttgaaatat atatatatat atatatatat atatatatat atatatatat atatatatat
95101 atatacatgt tggaatggct aaagtaagct aattaacatc tgcattacct cacatactta
95161 ttttttttgtg gtgcgaacac ttgaaatcta ctcttagtga ttttcaagaa tataatgcat
95221 tgttattaac tacagtcaat agatcatagg tctattcaag ttcaagtcac agatctcttg
95281 aaattactcc tcctgtctaa ctgaaatttt gtgtcctttg accaacatct ccccagttcc

95341 cctacgctca acatcactaa tcatcaagga aatgcaaatc gaaatcatga tgagtgtcat
95401 ctcacacctg ttagaatggc cattatcaaa aagacaagtg ttggtgggga tgtggaaaaa
95461 gggaactctt gcccaccgtt ggtgggaacg tagatcagta cagtcattat ggaaaacagg
95521 atggaggttc ctcaaaaaca caaagatcaa ttacaaaaca aaatactata tgttttacaa
95581 atgtactaca actcaatttg gtatgtatta caaatcaaaa tactacatga ttgctggcaa
95641 tcccactctg gagatagatc caaagaaaat ggaaaatgaa atcggtatgt caaagaggta
95701 ccagccctcc caaattcatt acagcattat tcacaacaga caaggtatgg catcaaccta
95761 agtgtccatc aacataaacg cccataaaga aaagtggtgc acatacacaa tggaacacta
95821 ttcagcattt agaagagaaa tcctgtcatt tgtgacaaca tgaacaaacc tggagaactt
95881 tatgctaaat gaaataagcc aggcacagaa agacacatac tgcatcctct cacttataca
95941 tagcatctga aaagttgaac tcctatttcc ttctttataq ttttgtgtat tttccaaatt
96001 ttctaaacca aaaatattca tctttataat caggggagaa aactaaggaa taatcatttt
96061 ataatcctaa acatgctttt aaaqcattta tttcactgta atgtattctt ttcccatcca
96121 gtcatacatg ggcccaagga gctggccttc cctgctcggc agcctgatgt tcaaggggat
96181 gggggagggg gacggtgcag tagatcatgc tttgcaaagc tgtgcaaatc ttttttttt
96241 tttttgaga cggagtctcg ctctgtcgcc cagggctgga tgcagtggca cgatctttggc
96301 tcactgcaac ctccgcctcc caggttcaca ccattctcct gcctcagcct cccgagtagc
96361 tgggattaca ggcgcccgcc accacacccg gctaattttt gtattttagt agagacgggg
96421 tttcatcgtg ttagccagga cggtctcaat ctcctgacct cgtgatccac ccgcctggc
96481 caaagtgctg ggattacagg cgtgagccac ggcgcccggc caaagctgtg caaatcttga
96541 gttaataaac atgttcccca aatccaaaag ccaatattga ctattgcttg gttaactgtt
96601 ttgcatggat aagtggttaa aggagtattt ggtttccaat ttctgcaaag ggaataaaag
96661 ttttaaaagc gtgaactaag atttcctata ctatgctatt ctatagtagg tttttatgcc
96721 aaaacctcta ctaggctgaa aggataattt gatttatggt tgagacattg ttgggcctga
96781 tttaaagccc agagtcaagc ccagagagga ttctcttaaa tatgtgcaat gggtattttt
96841 aaattagcat tatggcgtta ttaatatttc atttatcctg agagcattta cctgacaacg
96901 taaattatgt gtaacacagc tgagaaagcca caaaggatcc aaaaagatgt cacgaagtcc
96961 acgaagagaa gctttgccag agaaaggcac actaccagcc gcgtgagctg gcctcatcaa
97021 agcaaaaaag tcagaaaatt atgtaaacca gactcaagaa ctcaaaaata cagtcgtttg
97081 agaacattgg taagagtgca aactgctcac cccagctcaa tcaccctgg tccagcaacg
97141 gcagaaagcc aaggtcaagg agtcacatga cctgaagaga caccccccac caccaccacc
97201 accctccaag ccctgcccct ggccagtggg acaaaccaca tgaccctgg gattcagtat
97261 tcagtcaggt tctgtgttct gtatggggag gtagaagaag gcaccagatc atcaggaaat
97321 ctggactgga aatggccaaa gctgaacaca tctgagtacc tgaagggtaa gcttaaggtg
97381 tcaaagcagc catggtgagg cagaaagaac cttgagcttg gggccccaag tttatgctga
97441 cccactagca gccaacaaaa cctccctcag cctcagtttg ctcaatctga aactgtgagt
97501 aagaggctct gactccagag aggtggtgca agttcaatga gaagggqttg ctgatggtcc
97561 agatggacag atgcaaagca ctgcttttctg ttttgtctt tgttttgata caggattctc
97621 tctgtcatcc aggctggtgt gcagtggtgt caatagctca ctgcagcctg gacctcctcc
97681 ggctcaagtg atcctcccac ctcagccacc caactagctc agactatagg aaaaagagtc
97741 atgcaccacc atgcctggct aatttttaaa aaaaaaNttt tggagacatg agatctcact
97801 attttgtcca ggccaatctc gaactcctgg cctcaagcaa tcctcctctc tcagcctccc
97861 aaagtgcttg gattagaggg gtgagctacc atgcccagca aaggcattgt taaattcagg
97921 aatgaatgac caccttgttc cccaaaacac tagacaagag aaccattctc tacgcacaga
97981 tctccctggc caccacgtgt aagcagcagt gaatattcca taggtggaac tggctactgt
98041 gaagaaagaa aactccagaa aagctaccct cactccaaga agtagcctgg accccacgtg
98101 cgtgacagca gcctggggag aaggctccac tcccaccagc aatgccaagg acagagcagc
98161 agcagccgtc catccccaca gttatggtga acacagccac agagcagcct gcttttttca
98221 tgtatagcca cacacaggtg gcaatggcag cagacgtaac tggctgcct tcctcccttа
98281 tggaaggaaa catatttttg cttgggtgtt ctgcctgccc ccacatgacc caYggaggat
98341 gaccagcccc aacaccagtg taaatcctat cactgggcac catctcttct caccacggat
98401 tggtttaggg aagggcacat gatataattc tggtcagtct aacactcggg gaagcgagct
98461 agaggacttc taggaaaagt gttggctgat gaagaaaggc catagagtag tagtcctgtc
98521 tgtgtggcac ttggaactgt gagagccatc

[0269] Following are cDNA sequences for *PSMB1* (SEQ ID NO: 5), *TBP* (SEQ ID NO: 6), *PDCD2* (SEQ ID NO: 7 and 8), *ELP3* (SEQ ID NO: 9), *CHDC1* (SEQ ID NO: 10), and *ERG* (SEQ ID NO: 11 and 12).

PSMB1 cDNA sequence (SEQ ID NO: 5)

NM_002793 Homo sapiens proteasome (prosome, macropain) subunit, beta type, 1 (PSMB1), mRNA

```
   1 aaggcagcca tctcgccgtg agacagcaag tgtcgcgcag ccgtgcgatg ttgtcctcta
  61 cagccatgta ttcggctcct ggcagagact tggggatgqa accgcacaga gccgcgggcc
 121 ctttgcagct gcgatttttcg ccctacgttt tcaacggagg tactatactg gcaattgctg
 181 gagaagattt tgcaattgtt gcttctgata ctcgattgag tgaagggttt tcaattcata
 241 cgcgggatag ccccaaatgt tacaaattaa cagacaaaac agtcattgga tgcagcggtt
 301 ttcatggaga ctgtcttacg ctgacaaaga ttattgaagc aagactaaag atgtataagc
 361 attccaataa taaggccatg actacggggg caattgctgc aatgctgtct acaatcctgt
 421 attcaaggcg cttctttcca tactatgttt acaacatcat cggtggactt gatgaagaag
 481 gaaaggcggc tgtatacagc tttgatccag tagggtctta ccagagagac tccttcaagg
 541 ctggaggctc agcaagtgcc atgctacagc ccctgcttga caaccaggtt ggttttaaga
 601 acatgcagaa tgtggagcat gttccgctgt cctggacag agccatgcgg ctggtgaaag
 661 atgtcttcat ttctgcggct gagagagatg tgtacactgg ggacgcactc cggatctgca
 721 tagtgaccaa agagggcatc agggaggaaa ctgtttcctt aaggaaggac tgatctgtgt
 781 gctctatca ccaatcagtt cagacctggt tgattttgta ctttggaact gtaccttgga
 841 tggttttgtt tattaaaaga gaaacctgaa gt
```

TBP cDNA sequence (SEQ ID NO: 6)

NM_003194 Homo sapiens TATA box binding protein (TBP), mRNA

```
   1 ggttcgctgt ggcgggcgcc tgggccgccg gctgtttaac ttcgcttccg ctggcccata
  61 gtgatctttg cagtgaccca gcagcatcac tgtttcttgg cgtgtgaaga taccccaagg
 121 aattgaggaa gttgctgaga agagtgtgct ggagatgctc taggaaaaaa ttgaatagtg
 181 agacgagttc cagcgcaagg gtttctggtt tgccaagaag aaagtgaaca tcatggatca
 241 gaacaacagc ctgccacctt acgctcaggg cttggcctcc cctcagggtg ccatgactcc
 301 cggaatccct atctttagtc caatgatgcc ttatggcact ggactgaccc cacagcctat
 361 tcagaacacc aatagtctgt ctattttgga agagcaacaa aggcagcagc agcaacaaca
 421 acagcagcag cagcagcagc agcagcagca gcagcagcag cagcagcagc agcagcagca
 481 gcagcagcag cagcagcagc agcagcagca gcagcagcag gtggcagctg cagccgttca
 541 gcagtcaacg tcccagcagg caacacaggg aacctcaggc caggcaccac agctctctcca
 601 ctcacagact ctcacaactg caccctgcc gggcaccact ccactgtatc cctccccat
 661 gactcccatg acccccatca ctcctgccac gccagcttcg gagagttctg ggattgtacc
 721 gcagctgcaa aatattgtat ccacagtgaa tcttggttgt aaacttgacc taaagaccat
 781 tgcacttcgt gcccgaaacg ccgaatataa tcccaagcgg tttgctgcgg taatcatgag
 841 gataagagag ccacgaacca cggcactgat tttcagttct gggaaaatgg tgtgcacagg
 901 agccaagagt gaagaacagt ccagactggc agcaagaaaa tatgctagag ttgtacagaa
 961 gttgggtttt ccagctaagt tcttggactt caagattcag aatatggtgg ggagctgtga
1021 tgtgaagttt cctataaggt tagaaggcct tgtgctcacc caccaacaat ttagtagtta
1081 tgagccagag ttatttcctg gtttaatcta cagaatgatc aaacccagaa ttgttctcct
1141 tatttttgtt tctggaaaag ttgtattaac aggtgctaaa gtcagagcag aaatttatga
1201 agcatttgaa aacactctacc ctattcctaaa gggattcagg aagacgacgt aatggctctc
1261 atgtaccctt gcctccccca ccccctttctt ttttttttct taaacaaatc agtttgtttt
1321 ggtaccttta aatggtggtg ttgtgagaag atggatgttg agttgcaggg tgtggcacca
1381 ggtgatgccc ttctgtaagt gcccaccgcg ggatgccggg aaggggcatt atttgtgcac
1441 tgagaacacc gcgcagcgtg actgtgagtt gctcataccg tgctgctatc tgggcagcgc
1501 tgcccattta tttatatgta gattttaaac actgctgttg acaagttggt ttgaggaga
1561 aaacttaag tgttaaagcc acctctataa ttgattggac tttttaattt taatgttttt
1621 ccccatgaac cacagttttt atatttctac cagaaaagta aaaatctttt ttaaaagtgt
1681 tgttttttcta atttataact cctaggggtt atttctgtgc cagacacatt ccaccttctcc
1741 agtattgcag gacagaatat atgtgttaat gaaaatgaat ggctgtacat attttttttct
```

```
1801 ttcttcagag tactctgtac aataaatgca gtttataaaa gtgttaaaaa aaaaaaaaaa
1861 aaaaaaa
```

PDCD2 cDNA sequence 1 (SEQ ID NO: 7)

NM_002598 Homo sapiens programmed cell death 2 (PDCD2), transcript variant 1, mRNA

```
   1 tcttgctttc cggcccggcg cccgatttcc gccttccgac ccagctgtgg gctgcgcccc
  61 acgccagccc gcgccccgca tggctgccgc cggggccagg cctgtggagc tgggcttcgc
 121 cgagtcggcg ccggcgtggc gactgcgcag cgagcagttc cccagcaagg tgggcgggcg
 181 gccggcatgg ctgggcgcgg ccgggctgcc gggggcccag gccctggcct gcgagctgtg
 241 cggccgcccg ctctccttcc tgctgcaggt gtatgcgccg ctgcctggcc gcccggacgc
 301 cttccaccgc tgcatcttcc tcttctgctg ccgcgagcag ccgtgctgtg ccggcctgcg
 361 agtttttagg aatcaactac ccaggaaaaa cgatttttac tcatatgagc caccttctga
 421 gaatcctccc ccagaaacag gagaatcagt gtgtctccag cttaagtctg gtgctcatct
 481 ctgcagggtt tgtggctgtt taggccccaa aacgtgctcc agatgccaca aagcatatta
 541 ctgcagcaag gagcatcaga ccctagactg gagattggga cataagcagg cttgtgcaca
 601 accagatcat ctggaccata taattccaga ccacaacttc ctttttccag aatttgaaat
 661 tgtaatagaa acagaagatg agattatgcc tgaggttgtg gaaaaggaag attactcaga
 721 gattataggg agcatgggtg aagcacttga ggaagaactg gattccatgg caaaacatga
 781 atccagggaa gataaaattt ttcagaagtt taaaactcag atagcccttg aaccagaaca
 841 gattcttaga tatggcagag gtattgcccc catctggatt tctggtgaaa atattcctca
 901 agaaaaggat attccagatt gcccctgtgg tgccaagaga atattggaat tccaggtcat
 961 gcctcagctc ctaaactacc tgaaggctga cagactgggc aagagcattg actggggcat
1021 cctggctgtc ttcacctgtg ctgagagctg cagcttgggt actggctata cagaagaatt
1081 tgtgtggaag caggatgtaa cagatacacc gtaaaggcat cttaaagcct tgaaaaatgt
1141 taataatctt ttatacctg caattccatt tctgggattt tatcctaagg aaatacttat
1201 accaaaaata gaggtgcaga gatgttgaca gattgcttac acagtgtcta cttattagtg
1261 aaacaaaagt gtccagtgac agggaattaa ataaattttg gtacatccac a
```

PDCD2 cDNA sequence 2 (SEQ ID NO: 8)

NM_144781 Homo sapiens programmed cell death 2 (PDCD2), transcript variant 2, mRNA

```
   1 tcttgctttc cggcccggcg cccgatttcc gccttccgac ccagctgtgg gctgcgcccc
  61 acgccagccc gcgccccgca tggctgccgc cggggccagg cctgtggagc tgggcttcgc
 121 cgagtcggcg ccggcgtggc gactgcgcag cgagcagttc cccagcaagg tgggcgggcg
 181 gccggcatgg ctgggcgcgg ccgggctgcc gggggcccag gccctggcct gcgagctgtg
 241 cggccgcccg ctctccttcc tgctgcaggt gtatgcgccg ctgcctggcc gcccggacgc
 301 cttccaccgc tgcatcttcc tcttctgctg ccgcgagcag ccgtgctgtg ccggcctgcg
 361 agtttttagg aatcaactac ccaggaaaaa cgattttttac tcatatgagc caccttctga
 421 gaatcctccc ccagaaacag gagaatcagt gtgtctccag cttaagtctg gtgctcatct
 481 ctgcagggtt tgtggctgtt taggccccaa aacgtgctcc agatgccaca aagcatatta
 541 ctgcagcaag gagcatcaga ccctagactg gagattggga cataagcagg cttgtgcaca
 601 accagatcat ctggaccata taattccaga ccacaacttc ctttttccag aatttgaaat
 661 tgtaatagaa acagaagatg agattatgcc tgaggttgtg gaaaaggaag attactcaga
 721 gattataggg agcatgggta agcagtttca ggacttcatt cattaagtgg ttaaacataa
 781 tacttggaag aaagggctcc atgtgcctag aagagaggta ctgagaggaa gactcacttt
 841 ggaggctgta gcatacaatt ttcagatatt gcctcaggta aaaatatact tcctggactt
 901 tgttttctga cacataagag gtgtgttctg ctccctgtaa agacaaggat gggtatccag
 961 atggtcccat gagtagggct gcacaagatg ctggaggctt ggtaagttcc tctgggtcgc
1021 agatcggttt ctcgggtcgg gatagtgtga gtgcctagca cagtgtcggg cacgcagaag
1081 ggcccctaa aagtttctct ttcatctggc cagttttaga tacacaattt tgtcagttta
1141 cttacagtgc atacttcttg gtagtacttg tgctgaccaa gtatcttaga ggcttatttt
1201 attatagtag ccaacattta tccagcactt acctatata aagggctgtt tgtgcatgag
1261 ctcattaaaa tcgtgacagc agaccaatga gtgagaaact gcccatttt gaaggtgagg
1321 aaattgaggt tctgggtata actttctttg gtcacataat attaaatttt acaatttgag
1381 ccttgagcca tacacaaaac caccacaaaa ttagatttat agactcaaaa tgaaaacatc
```

```
1441 agcttactgg tttgtagttc ataccagtca tacattccaa aacatgtttt gagtcttact
1501 ctgtgcctga ccttgtgctt gataacaggg atataatggg aagcaacact ccagtggtca
1561 gatgctcaca gtcttatgga ggagcccaaa taatatctgg ggaagttaaa gtccatataa
1621 tgactgataa gagtacaata caggtgccat gggaacacgt gacatcactg aagactgcct
1681 ggaaggggcc gcgcgtgtgt tcatgcctat acgataaaca tgatacataa tgaaaatgct
1741 tatcttagg agaaaggaga gcctagagta gcaggatcaa ggatgaaagc tggacttcaa
1801 atatgccttg ttagtgtaaa tgtgactgtg gaactgtatg agtattttaa gattatggag
1861 taaagtaagt tttaaaaagc agtccctaat catcaaaagt aaaaaactct tgatgtagtc
1921 atataaccac actaagaact cttccaggtg acttcaaaac ataggacagt acatctctag
1981 tagaatatgc cctgagaatg aaaagaatgt aacagtgtta gtattttgaa taaacatgtt
2041 attactaaaa aaaaaaaaaa aaaaaa
```

ELP3 cDNA sequence (SEQ ID NO: 9)

NM_018091 Homo sapiens elongation protein 3 homolog (S. cerevisiae) (ELP3), mRNA

```
   1 gcagaaatga ggcagaaagcg gaaaggagat ctcagccctg catgagctgat gatgctgact
  61 ataggagatg ttattaaaca actgattgaa gcccacgagc agggggaaaga catcgatcta
 121 aataaggtga aaaccaagac agctgccaaa tatggccttt ctgcccagcc ccgcctggtg
 181 gatatcattg ctgccgtccc tcctcagtat cgcaaggtct tgatgcccaa gttaaaggcg
 241 aaacccatca gaactgctag tgggattgct gtcgtggctg tgatgtgcaa accccacaga
 301 tgtccacaca tcagttttac aggaaatata tgtgtatact gccctggtgg acctgattct
 361 gattttgagt attccaccca gtcttacact ggctatgagc caacctccat gagagctatc
 421 cgtgccagat atgacccttt cctacagaca agacaccgaa tagaacagtt aaaacaactt
 481 ggtcatagtg tggataaagt ggagtttatt gtgatgggtg gaacgtttat ggcccttcca
 541 gaagaataca gagattattt tattcgaaat ttacatgatg ccttatcagg acatacttcc
 601 aacaatattt acgaggcagt caagtattct gagagaagcc tcacaaagtg tattggaatt
 661 actattgaaa ccagaccaga ttactgcatg aagcgacatt taagtgacat gttgacctat
 721 ggctgcacaa ggctggagat tggggtgcag agtgtttatg aagatgtggc tagagacacc
 781 aacagggcgc acactgtgaa ggcagtgtgt gagtcatttc acctggccaa agattccggt
 841 tttaaagtgg tggcccatat gatgcctgac ctgccaaacg tgggactaga aagagacatt
 901 gaacagttca cagagttttt tgagaaccct gcttttcgtc ccgatgggct gaaactctat
 961 cctaccctgg tgattcgtgg gaccgggctt tatgagcttt ggaaatcagg aagataataag
1021 agttactctc ctagtgacct ggttgaattg gtggctcgga tcctagccct cgtgcctcca
1081 tggactcgag tgtaccgagt acagagggat attccaatgc ctttagttag ctcaggagta
1141 gagcatggta acctgagaga gctggccatt gcaagaatga aagacctcgg aatacagtgt
1201 cgagatgtga gaaccagaga agttggaatc caagaaattc atcacaaagt acaggccatac
1261 caggttgaat tggtaaggag agattatgtt gcaaatggtg gctgggaaac atcttgtca
1321 tacgaagacc cagatcaaga catttgatt ggcctcctac gattacgcaa gtgttcagaa
1381 gaaactttcc gtttcgaatt gggtggaggt gtctccatag tacgagagct gcatgtgtat
1441 ggtagtgtgg tccctgtgag cagccgggat cctactaaat ttcagccata gggatttggc
1501 atgctgctga tggaggaagc agaaagaata gctagagaag aacatgggtc tgggaaaatc
1561 gctgtgatat cagggtcgg caccaggaat tattatagaa agatcggcta cagattacaa
1621 ggcccgtaca tggtgaagat gctgaaataa tggccacacc agtccactct tctgcagtat
1681 cctccctggc agaacacgga gaatcaggat ttcttaaata ctcaacagag aggctgagca
1741 gagcaaatgg ggggcttcac cctcatcccg cagctgcaga gactggaaac tgccttcaag
1801 gccacggctg gtcatctgct gaccacaccc cagatccgcc ctttcctgcg tgcaccccaa
1861 aaaatcactt gcgttttga ggcttaaatc atctatccag tttctacatt ttgcatgagg
1921 cctgcaggtg gcctattttg actcagacgg tgaaaaaagc aaattaactc attggagcac
1981 catacctcat gcaataaaac tgattgtcat tcgaggagca aacttaagag tagtttattt
2041 atataccctg gggacagaaa gtcaggttga aacaggaaaa ccaccagact ctaatctcag
2101 ccctttaacg acatacgcat tggagcgcaa gttaggaaaa tgagctttg ttttcatgga
2161 aatcattctg attacagtgc tgatgtttag aaataaatag cagtgtgact gggaaagagg
2221 aattgcagtt gtgggggtgt gagcctggca gcagccacgc agcagcctct ccaggcggg
2281 agtctaccat ccgagacggc gatgacaaag agcttcattc cacattcttt gttatctcta
2341 cttcccaccc tcttggcaac tacagagcag tgtggcagc cccaagtgtg gtccccagag
2401 agcgtttggc tttcctgtct gtcatatcctg agcgggtgga gtctcaggtt gtgtgcccct
2461 aaatcaagat ttgcttccac agaagccatt acttgcaatt ttttttttt tttctgagaa
2521 agtctcgctg tgtcacccag gctggagtgc agtggcgcaa tcctcactgca tcctccgcct
2581 ccgggttca agcgattctc ccgcctcagc ctcctgagta gctgggatta caggcaccog
2641 ccgctgctaa ttttgtattt tttagtagag atggggggtt caccatattg gtcaggctgg
2701 tctcgaactc ctgacctcag gtgatcaacc caccttggcc tccctaaatg ccgggattac
```

```
2761 aggcatgagc caccgctccc agcctttgat tttttaaggt ggattttggt tgttataaat
2821 ggagaaaggt aagagttcaa gttcaacccg tgtgtgaaag caaaacaatg gaaaacagga
2881 ttggcttctt caaaggctcc tcttgtagaa ctgcctcttt gaaatttcga ggtaatctac
2941 tttcggagact ctgcctggag agggtcagtt cctaagttaa aagcatcgct taaccttggc
3001 tcctgtggca ttttacaaag gtttaaagga attgattcct ctgaaaatga
3061 aaagtctttta acatataaaa aaaaaaaaaa aaaaa
```

CHDC1 cDNA sequence (SEQ ID NO: 10)

NM_015116 Homo sapiens calponin homology (CH) domain containing 1 (CHDC1), mRNA

```
   1 ccgcagtcct tagcttcccg gggacaggaa accttcaaga ccgagctgcc acggccgcct
  61 ccccgcccgc ccccattct acgcgcctgc ccacacccctc ctcccctcct tccagcgcct
 121 ttcggtggag cactgcggca ctcagcccga gctgccgttt tcccctcgcg gggaacgctg
 181 tgaccccccc gcaggagcgg cgggcgggg tgggggggcc cgggagaaga tggcgacgcc
 241 gggaagcgaa ccccaacctt tcgtcccggc cctttcggta gctactctgc acccacttca
 301 tcatccccac caccaccacc accaccatca gcaccacgga ggaaccggcg cccccggcgg
 361 ggcgggtggt ggcggcggtg gcagcggggg cttcaacctg cccttgaacc ggggtctgga
 421 gcgcgcgctt gaggaggcgg ccaactccgg ggggctgaac ctgagcgcca ggaaattgaa
 481 ggaatttccc cgtaccgcag ccccgggga tgacctctcg gacacggtgc aggcagactt
 541 atctaaaaac agactggttg aagttccaat ggaattgtgc cattttgtat cactggaaat
 601 tcttaatctg tatcacaact gtatcagagt cattcctgag gccatcgtta atctgcagat
 661 gctgacttac ctgaacttga gtcgaaatca gctgtccgcc ctgcctgcct gcctgtgtgg
 721 tctgcctctc aaagtcttaa tcgcaagtaa caacaaactt ggatcattac cagaagagat
 781 aggtcagctc aaacagttaa tgqaqctgga tgtcaqctgc aacgaqatca cagcgttcgc
 841 ccagcagata ggtcagttga aatctctacg agaactgaat gtcagaagaa attacctaa
 901 agttttacca caagaactag tagatcttcc cttggtaaag tttgactttt cctgcaacaa
 961 agtgctcgtg attccaattt gttttagaga gatgaagcag ctgcaagtgt tactacttga
1021 gaataaccct ctgcagtctc ctccagcaca gatttgcaca aagggcaaag ttcacatatt
1081 taagtatctg agcatacaag catgccagat taagacagct gactcccttt atctccacac
1141 catggagagg ccacatttac accagcacgt ggaagatggc aagaaggatt ctgattcggg
1201 agttggaagt gataatggag ataagcgatt atctgccacc gagcctttctg acgaagacac
1261 tgttagcctc aatgtgccaa tgtcaaacat catggaagaa gaacagatca tcaaggagga
1321 ctcgtgccat cgccttagcc ccgttaaagg ggaatttcat caggaatttc aaccggagcc
1381 ttcccttttg ggtgacagca ccaactcagg agaagaaaga gaccagttta ctgatagagc
1441 agatggtctc cattcggaat ttatgaacta taaggcaagg gcagaagact gtgaagagct
1501 gttacggata gaagaggatg tgcactggca aactgagggc ataataagtt catccaaaga
1561 tcaggacatg gatatagcaa tgatcgagca gctgagagaa gcagtagatt tgctgcaaga
1621 tcccaatgga ttaagcacag atattacaga gagaagtgtt ttaaacctat atcctatggg
1681 atcagcagaa gccttagaat tacaagattc tgcactgaat ggtcaaatac agctggagac
1741 atctccggtg tgtgaggtgc aaagtgatct aacattacag agtaacggga gccagtattc
1801 tccaaatgag attagagaga actcccctgc agtctctcct accacaaaca gcacagctcc
1861 atttggcctg aagcctcgat cagtgttttt aagacctcag agaaatttgg aatctataga
1921 cccgcagttt acaatccgga ggaaaatgga gcagatgaga gaagagaaag agctggtgga
1981 acaacttcgt gagagcattg agatgagatt gaaggtcagt ctcacgaag acctgggggc
2041 agccctcatg gatggtgtcg tcctctgcca tctggtcaac cacatcgcc cacggtcggt
2101 tgcaagcatc catgtcccat caccagcggt tcccaaactt agcatggcca aatgccagag
2161 aaatgtggaa aacttttgg aagcgtgccg aaaattagga gtaccagagg ctgaccctg
2221 ctctccgtgt gacatcctgc agttggattt tcgtcacatt cgaaagactg ttgacactct
2281 gctggcactc ggggagaaag ccccaccacc aacttctgcc ctccgctcca gggaccttat
2341 aggcttctgt cttgtccata ttctctttat agtgctggtc tatatcactt accactgaa
2401 tgctctgtcc gcataacgtc tgcacgtgca tccaaacgct gtgctctgtc gccctcaacc
2461 tttgcagggt ccttcctacc tttgagcctt tgccttgcaa acttccatcc ctgtcatgtc
2521 ttcagttatc tctcgagttt tgaagctgaa cagtagcaaa tcagattttc cagaagcaca
2581 aactttgtag aatacagttt agtataattc ctctcactta ctgaaataca acgacgacga
2641 ctgcaaagtg tatgcacacc gcatgcttcc tcatccacat agtgccagca gcagtgccac
2701 gcagttcctc ctctccctcc cggtgagctg ctgccctggg cagaggggag gagaatttcca
2761 ggacaagagt gtcaaggaca gggatttagc atatggaagt ctttccttg ggtcagtatt
2821 gaactagaat tctaattcgg gactgggcaa ttgagctgta taggggccac cttgcaggga
2881 ggacagaaaa ctaacatttt ggcccaactt gatctataca aaacttaaat aataccacta
2941 ctgaccaagt tggacgtgta cacgtactca cactgccttg atggccattc gattggattc
```

```
3001 ctcccaaatt tcctaaaaag ggagccgcga agggcgctgg gcagtgtggc cgccaacttc
3061 caccccggca agccccctctg tcctatgcag aagggcgctc cagggaagga agtgtcgttg
3121 ctgttagagc ctcacgtgga ggagtcactt aaacaccagt tttttactgc ttaattcctt
3181 gttaggtctt ctcttgaggc tcttagaaaa gcgtttttca gagagatttc tatttttgaa
3241 caatggaacg gatcactgct tttttgccac atcacatagt aactgccggt ccagaatgtg
3301 acggattcga ctctattcat tttcaaataa agccatgagc cgtggaacat tctggtgtct
3361 ggtgcttggg ttatgatggc aggagtcaag aagaagatta ctttcattct agaagaatgt
3421 agtttctcta attatttgaa atgttcattt agcctttgat tttcactgat attaactagc
3481 aaactgcttt aagtcagctc aaaggattat atagtaacta tatctgcatt tggagcaatg
3541 tgatcagttt gcatttaaaa ggaaaaaaaa gaattttatc ttagccagaa tgtccctgga
3601 ttcaggggtg tctttgtata atatgagagg gccttgttcc aaggtcaagg cagcctcctt
3661 attttacatg ctgtttgcca aatcttgttt cttagcttgg ggagatgatg gacttagctt
3721 cctcaagata aatttctagt ttattaagat gcaaacagct ctcatagatg gctactacga
3781 agaaaatctt atttttctga acattttcat gaatccaggg gacttgaaaa tatggaagac
3841 ccacatagtt agaagaatat atttataaag attccttgct gctaagtcag atcagatttg
3901 ctaacaggaa gcattctttа catgacagta tcttgagtta tgtgagtttt ttttcctcct
3961 gactttgtgt tgattggtga aatgcagggt atgtggaagt tatctaatta acctcagttg
4021 tatatgaata acccacagat gtactgaatt acttttggtg ctatcttgta ctcttcaatc
4081 tgtaacacaa taaaatccct ttgtacgatg tctaatgagc accctgagcc ataaattgct
4141 taataaacac attttgggtg att
```

ERG cDNA sequence 1 (SEQ ID NO: 11)

NM_182918 Homo sapiens v-ets erythroblastosis virus E26 oncogene like (avian), (ERG), transcript variant 1, mRNA

```
   1 aatctcatcc gctctaaaca acctcatcaa aactactttc tggtcagaga gaagcaataa
  61 ttattattaa catttattaa cgatcaataa acttgattgc attatggcca gcactattaa
 121 ggaagcctta tcagttgtga gtgaggacca gtcgttgttt gagtgtgcct acggaacgcc
 181 acacctggct aagacagaga tgaccgcgtc ctcctccagc gactatggac agacttccaa
 241 gatgagccca cgcgtccctc agcaggattg gctgtctcaa ccccagccta gggtcaccat
 301 caaaatggaa tgtaacccta gccaggtgaa tggctcaagg aactctcctg atgaatgcag
 361 tgtggccaaa ggcgggaaga tggtgggcag cccagacacc gttgggatga actacggcag
 421 ctacatggag gagaagcaca tgccaccccc aaacatgacc acgaacgagc gcagagttat
 481 cgtgccagca gatcctacgc tatggagtac agaccatgtg cggcagtggc tggagtgggc
 541 ggtgaaagaa tatggccttc cagacgtcaa catcttgtta ttccagaaca tcgatgggaa
 601 ggaactgtgc aagatgacca aggacgactt ccagaggctc accccagct acaatgccga
 661 catcctctct tcacattctc actacctcag agagactcct cttccacatt tgacttcaga
 721 tgatgttgat aaagccttac aaaactctcc acggttaatg catgctagaa acacaggggg
 781 tgcagctttt attttcccaa atacttcagt atatcctgaa gctacgcaaa gaattacaac
 841 taggccagat ttaccatatg agccccccag gagatcagcc tggaccggtc acggccaccc
 901 cacgcccag tcgaaagctg ctcaaccatc tccttccaca gtgcccaaga ctgaagacca
 961 gcgtcctcag ttagatcctt atcagattct tggaccaaca agtagccgcc ttgcaaatcc
1021 aggcagtggc cagatccagc tttggcagtt cctcctggag ctcctgtcgg acagctccaa
1081 ctccagctgc atcacctggg aaggcaccaa cggggagttc aagatgacgg atcccgacga
1141 ggtggcccgg cgctggggag agcggaagag caaacccaac atgaactacg ataagctcag
1201 ccgcgccctc cgttactact atgacaagaa catcatgacc aaggtccatg ggaagcgcta
1261 cgcctacaag ttcgacttcc acgggatcgc ccaggccctc ccagcccacc ccccgagtc
1321 atctctgtac aagtacccct cagacctccc gtacatgggc tcctatcacg cccacccaca
1381 gaagatgaac tttgtggcgc cccacccctc agccctcccc gtgcatctt ccagttttt
1441 tgctgcccca aacccatact ggaattcacc aactgtgggt atataccccca ccactaggct
1501 ccccaccagc catatgcctt ctcatctggg cacttactac taaagacctg gcggaggctt
1561 ttcccatcag cgtgcattca ccagcccatc gccacaaact ctatcggaga acatgaatca
1621 aaagtgcctc aagaggaatg aaaaaagctt tactgcggct ggggaaggaa gccggggaag
1681 agatccaaag actcttggga gggagttact gaagtcttac tacagaaatg aggaggatgc
1741 taaaaatgtc acgaatatgg acatatcatc tgtggactga ccttgtaaaa gacagtgtat
1801 gtagaagcat gaagtcttaa ggacaaagtg ccaaagaaag tggtcttaag aaatgtataa
1861 actttagagt agagtttgga atcccactaa tgcaaactgg gatgaaacta aagcaataga
1921 aacaacacag ttttgaccta acataccgtt tataatgcca ttttaaggaa aactacctgt
1981 atttaaaaat agaaacatat caaaaaaaaa aaaaaa
```

ERG cDNA sequence *2* (SEQ ID NO: 12)

NM_004449 Homo sapiens v-ets erythroblastosis virus E26 oncogene like (avian), (ERG), transcript variant 2, mRNA

```
   1 atgattcaga ctgtcccgga cccagcagct catatcaagg aagccttatc agttgtgagt
  61 gaggaccagt cgttgtttga gtgtgcctac ggaacgccac acctggctaa gacagagatg
 121 accgcgtcct cctccagcga ctatggacag acttccaaga tgagcccacg cgtccctcag
 181 caggattggc tgtctcaacc cccagccagg gtcaccatca aaatggaatg taaccctagc
 241 caggtgaatg gctcaaggaa ctctcctgat gaatgcagtg tggccaaagg cgggaagatg
 301 gtgggcagcc cagacaccgt tgggatgaac tacggcagct acatggagga gaagcacatg
 361 ccacccccaa acatgaccac gaacgagcgc agagttatcg tgccagcaga tcctacgcta
 421 tggagtacag accatgtgcg gcagtggctg gagtgggcgg tgaaagaata tggccttcca
 481 gacgtcaaca tcttgttatt ccagaacatc gatgggaagg aactgtgcaa gatgaccaag
 541 gacgacttcc agaggctcac ccccagctac aacgccgaca tccttctctc acatctccac
 601 tacctcagag agactcctct tccacatttg acttcagatg atgttgataa agccttacaa
 661 aactctccac ggttaatgca tgctagaaac acagatttac catatgagcc ccccaggaga
 721 tcagcctgga ccggtcacgg ccaccccacg ccccagtcga aagctgctca accatctcct
 781 tccacagtgc ccaaaactga agaccagcgt cctcagttag atccttatca gattcttgga
 841 ccaacaagta gccgccttgc aaatccaggc agtggccaga tccagctttg gcagttcctc
 901 ctggagctcc tgtcggacag ctccaactcc agctgcatca cctgggaagg caccaacggg
 961 gagttcaaga tgacggatcc cgacgaggtg gcccggcgct ggggagagcg gaagagcaaa
1021 cccaacatga actacgataa gctcagccgc gccctccgtt actactatga caagaacatc
1081 atgaccaagg tccatgggaa gcgctacgcc tacaagttcg acttccacgg gatcgcccag
1141 gccctccagc cccacccccc ggagtcatct ctgtacaagt acccctcaga cctcccgtac
1201 atgggctcct atcacgccca cccacagaag atgaactttg tggcgcccca ccctccagcc
1261 ctccccgtga catcttccag ttttttgct gccccaaacc catactggaa ttcaccaact
1321 gggggtatat accccaacac taggctcccc accagccata tgccttctca tctgggcact
1381 tactactaa
```

[0270] Following are amino acid sequences for *PSMB1* (SEQ ID NO: 13), *TBP* (SEQ ID NO: 14), *PDCD2* (SEQ ID NO: 15 and 16), *ELP3* (SEQ ID NO: 17), *CHDC1* (SEQ ID NO: 18), and *ERG* (SEQ ID NO: 19 and 20).

PSMB1 amino acid sequence (SEQ ID NO: 13)

NP_002784 Homo sapiens proteasome (prosome, macropain) subunit, beta type, 1 (PSMB1), protein

MLSSTAMYSAPGRDLGMEPHRAAGPLQLRFSPYVFNGGTILAIAGEDFAIVASDTRLSE
GFSIHTRDSPKCYKLTDKTVIGCSGFHGDCLTLTKIIEARLKMYKHSNNKAMTTGAIAA
MLSTILYSRRFFPYYVYNIIGGLDEEGKGAVYSFDPVGSYQRDSFKAGGSASAMLQPLL
DNQVGFKNMQNVEHVPLSLDRAMRLVKDVFISAAERDVYTGDALRICIVTKEGIREET
VSLRKD

TBP amino acid sequence (SEQ ID NO: 14)

NP_003185 Homo sapiens TATA box binding protein (TBP), protein

MDQNNSLPPYAQGLASPQGAMTPGIPIFSPMMPYGTGLTPQPIQNTNSLSILEEQQRQQQ
QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQAVAAAAVQQSTSQQATQGT
SGQAPQLFHSQTLTTAPLPGTTPLYPSPMTPMTPITPATPASESSGIVPQLQNIVSTVNLG

CKLDLKTIALRARNAEYNPKRFAAVIMRIREPRTTALIFSSGKMVCTGAKSEEQSRLAAR
KYARVVQKLGFPAKFLDFKIQNMVGSCDVKFPIRLEGLVLTHQQFSSYEPELFPGLIYR
MIKPRIVLLIFVSGKVVLTGAKVRAEIYEAFENIYPILKGFRKTT

PDCD2 amino acid sequence 1 (SEQ ID NO: 15)

NP_002589 Homo sapiens programmed cell death 2 (PDCD2), isoform 1, protein

MAAAGARPVELGFAESAPAWRLRSEQFPSKVGGRPAWLGAAGLPGPQALACELCGRP
LSFLLQVYAPLPGRPDAFHRCIFLFCCREQPCCAGLRVFRNQLPRKNDFYSYEPPSENPPP
ETGESVCLQLKSGAHLCRVCGCLGPKTCSRCHKAYYCSKEHQTLDWRLGHKQACAQP
DHLDHIIPDHNFLFPEFEIVIETEDEIMPEVVEKEDYSEIIGSMGEALEEELDSMAKHESRE
DKIFQKFKTQIALEPEQILRYGRGIAPIWISGENIPQEKDIPDCPCGAKRILEFQVMPQLLN
YLKADRLGKSIDWGILAVFTCAESCSLGTGYTEEFVWKQDVTDTP

PDCD2 amino acid sequence 2 (SEQ ID NO: 16)

NP_659005 Homo sapiens programmed cell death 2 (PDCD2), isoform 2, protein

MAAAGARPVELGFAESAPAWRLRSEQFPSKVGGRPAWLGAAGLPGPQALACELCGRP
LSFLLQVYAPLPGRPDAFHRCIFLFCCREQPCCAGLRVFRNQLPRKNDFYSYEPPSENPPP
ETGESVCLQLKSGAHLCRVCGCLGPKTCSRCHKAYYCSKEHQTLDWRLGHKQACAQP
DHLDHIIPDHNFLFPEFEIVIETEDEIMPEVVEKEDYSEIIGSMGKQFQDFIH

ELP3 amino acid sequence (SEQ ID NO: 17)

NP_060561 Homo sapiens elongation protein 3 homolog (S. cerevisiae) (ELP3), protein

MRQKRKGDLSPAELMMLTIGDVIKQLIEAHEQGKDIDLNKVKTKTAAKYGLSAQPRLV
DIIAAVPPQYRKVLMPKLKAKPIRTASGIAVVAVMCKPHRCPHISFTGNICVYCPGGPDS
DFEYSTQSYTGYEPTSMRAIRARYDPFLQTRHRIEQLKQLGHSVDKVEFIVMGGTFMAL
PEEYRDYFIRNLHDALSGHTSNNIYEAVKYSERSLTKCIGITIETRPDYCMKRHLSDMLT
YGCTRLEIGVQSVYEDVARDTNRGHTVKAVCESFHLAKDSGFKVVAHMMPDLPNVGL
ERDIEQFTEFFENPAFRPDGLKLYPTLVIRGTGLYELWKSGRYKSYSPSDLVELVARILA
LVPPWTRVYRVQRDIPMPLVSSGVEHGNLRELALARMKDLGIQCRDVRTREVGIQEIHH
KVRPYQVELVRRDYVANGGWETFLSYEDPDQDILIGLLRLRKCSEETFRFELGGGVSIV
RELHVYGSVVPVSSRDPTKFQHQGFGMLLMEEAERIAREEHGSGKIAVISGVGTRNYYR
KIGYRLQGPYMVKMLK

CHDC1 amino acid sequence (SEQ ID NO: 18)

NP_055931 Homo sapiens calponin homology (CH) domain containing 1 (CHDC1), protein

MATPGSEPQPFVPALSVATLHPLHHPHHHHHHHQHHGGTGAPGGAGGGGGGSGGFNL
PLNRGLERALEEAANSGGLNLSARKLKEFPRTAAPGHDLSDTVQADLSKNRLVEVPME
LCHFVSLEILNLYHNCIRVIPEAIVNLQMLTYLNLSRNQLSALPACLCGLPLKVLIASNNK
LGSLPEEIGQLKQLMELDVSCNEITALPQQIGQLKSLRELNVRRNYLKVLPQELVDLPLV
KFDFSCNKVLVIPICFREMKQLQVLLLENNPLQSPPAQICTKGKVHIFKYLSIQACQIKTA
DSLYLHTMERPHLHQHVEDGKKDSDSGVGSDNGDKRLSATEPSDEDTVSLNVPMSNIM
EEEQIIKEDSCHRLSPVKGEFHQEFQPEPSLLGDSTNSGEERDQFTDRADGLHSEFMNYK
ARAEDCEELLRIEEDVHWQTEGIISSSKDQDMDIAMIEQLREAVDLLQDPNGLSTDITER
SVLNLYPMGSAEALELQDSALNGQIQLETSPVCEVQSDLTLQSNGSQYSPNEIRENSPAV
SPTTNSTAPFGLKPRSVFLRPQRNLESIDPQFTIRRKMEQMREEKELVEQLRESIEMRLKV
SLHEDLGAALMDGVVLCHLVNHIRPRSVASIHVPSPAVPKLSMAKCRRNVENFLEACR
KLGVPEADLCSPCDILQLDFRHIRKTVDTLLALGEKAPPPTSALRSRDLIGFCLVHILFIVL
VYITYHWNALSA

ERG amino acid sequence 1 (SEQ ID NO: 19)

NP_891548 Homo sapiens v-ets erythroblastosis virus E26 oncogene like (avian), (ERG), isoform 1, protein

MASTIKEALSVVSEDQSLFECAYGTPHLAKTEMTASSSSDYGQTSKMSPRVPQQDWLS
QPPARVTIKMECNPSQVNGSRNSPDECSVAKGGKMVGSPDTVGMNYGSYMEEKHMPP
PNMTTNERRVIVPADPTLWSTDHVRQWLEWAVKEYGLPDVNILLFQNIDGKELCKMT
KDDFQRLTPSYNADILLSHLHYLRETPLPHLTSDDVDKALQNSPRLMHARNTGGAAFIF
PNTSVYPEATQRITTRPDLPYEPPRRSAWTGHGHPTPQSKAAQPSPSTVPKTEDQRPQLD
PYQILGPTSSRLANPGSGQIQLWQFLLELLSDSSNSSCITWEGTNGEFKMTDPDEVARRW
GERKSKPNMNYDKLSRALRYYYDKNIMTKVHGKRYAYKFDFHGIAQALQPHPPESSLY
KYPSDLPYMGSYHAHPQKMNFVAPHPPALPVTSSSFFAAPNPYWNSPTGGIYPNTRLPT
SHMPSHLGTYY

ERG amino acid sequence 2 (SEQ ID NO: 20)

NP_004440 Homo sapiens v-ets erythroblastosis virus E26 oncogene like (avian), (ERG), isoform 2, protein

MIQTVPDPAAHIKEALSVVSEDQSLFECAYGTPHLAKTEMTASSSSDYGQTSKMSPRVP
QQDWLSQPPARVTIKMECNPSQVNGSRNSPDECSVAKGGKMVGSPDTVGMNYGSYME
EKHMPPPNMTTNERRVIVPADPTLWSTDHVRQWLEWAVKEYGLPDVNILLFQNIDGKE
LCKMTKDDFQRLTPSYNADILLSHLHYLRETPLPHLTSDDVDKALQNSPRLMHARNTD
LPYEPPRRSAWTGHGHPTPQSKAAQPSPSTVPKTEDQRPQLDPYQILGPTSSRLANPGSG
QIQLWQFLLELLSDSSNSSCITWEGTNGEFKMTDPDEVARRWGERKSKPNMNYDKLSR
ALRYYYDKNIMTKVHGKRYAYKFDFHGIAQALQPHPPESSLYKYPSDLPYMGSYHAHP
QKMNFVAPHPPALPVTSSSFFAAPNPYWNSPTGGIYPNTRLPTSHMPSHLGTYY

[0271] Modifications may be made to the foregoing without departing from the basic aspects of the invention. Although the invention has been described in substantial detail with reference to one or more specific embodiments, those of skill in the art will recognize that changes may be made to the embodiments specifically disclosed in this application, yet these modifications and improvements are within the scope and spirit of the invention, as set forth in the aspects which follow. All publications or patent documents cited in this specification are incorporated herein by reference as if each such publication or document was specifically and individually indicated to be incorporated herein by reference.

[0272] Citation of the above publications or documents is not intended as an admission that any of the foregoing is pertinent prior art, nor does it constitute any admission as to the contents or date of these publications or documents. U.S. patents and other publications referenced herein are hereby incorporated by reference.

What is claimed is:

1. A method for identifying a subject at risk of osteoarthritis, which comprises detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in a nucleic acid sample from a subject, wherein the one or more polymorphic variations are detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-12;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(d) a fragment of a nucleotide sequence of (a), (b), or (c);

whereby the presence of the polymorphic variation is indicative of the subject being at risk of osteoarthritis.

2. The method of claim 1, which further comprises obtaining the nucleic acid sample from the subject.

3. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 170719500 to 170766500 in human genomic DNA.

4. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 229, 6310, 11840, 11870, 12064, 13392, 16354, 16559, 16935, 17616, 17737, 18321, 18453, 18811, 20020, 21662, 23197, 23446, 24339, 25504, 27174, 28008, 29294, 29759, 30832, 44512, 44850, 45884, 46345, 48589, 53371, 53911, 53990, 55152, 55667, 58952, 59315, 60029, 61477, 62988, 63090, 64021, 65685, 70220, 70323, 70959, 73436, 82945, 82958, 82961, 82964, 82965, 83006, 83025, 83034, 83074 ,83132, 83155, 83172, 83174, 83206, 83216, 83234, 83252, 83260, 83263, 83296, 83319, 83322, 83324, 83357, 83375, 83381, 83389, 83443, 83499, 83545, 83566, 83591, 83619, 83698, 83780, 83784, 83826, 83832, 83852, 86297, 86315, 86420, 86460, 86714, 86718, 86736, 86753, 86766, 88162, 88218, 88246, 88255, 88309, 88310, 88471, 88619, 88904, 89044, 90531, 90534, 90613 and 46252.

5. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 229, 6310, 16559, 18453, 25504, 27174, 30832, 44850, 45884, 48589, 61477, 82961 and 46252.

6. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 27963000 to 27983000 in human genomic DNA.

7. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 2 selected from the group consisting of 211, 473, 1536, 5639, 17186, 17335, 25029, 25111, 28811, 28863, 30809, 40985, 45147, 45282, 46168, 46328, 49077, 51925, 52141, 52168, 60852, 62468, 65572, 79089, 79541, 79790, 90843, 90978, 91052, 91131, 91132, 94439 and 94621.

8. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 2 selected from the group consisting of 40985, 46168, 51925 and 52168.

9. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 44962000 to 45013000 in human genomic DNA.

10. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 3 selected from the group consisting of 243, 10208, 15049, 15111, 15272, 15287, 15326, 15327, 17038, 19391, 21702, 22431, 22881, 27744, 32564, 32698, 33104, 33181, 33256, 33543, 35567, 40085, 40482, 45641, 46059, 48504, 48919, 49693, 49874, 50020, 50616, 50719, 55511, 65533, 70529, 75591, 77266, 80368, 82475, 92462, 92480, 95819 and 96275.

11. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 3 selected from the group consisting of 15111, 45641, 46059, 49693, 49874, 50020, 50719, 70529, 82475, 92462, 92480 and 96275.

12. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 38830000 to 38844000 in human genomic DNA.

13. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 4 selected from the group consisting of 231, 882, 960, 1194, 1530, 1673, 2096, 2285, 5873, 7256, 7988, 8222, 8381, 8814, 8915, 9642, 9902, 10619, 10927, 11032, 14377, 15608, 15928, 16296, 17598, 19272, 20084, 20577, 28051, 29466, 29530, 29987, 30012, 30322, 32216, 32516, 32544, 32746, 33137, 33538, 33798, 33802, 33964, 34132, 34210, 34317, 34499, 34753, 34845, 35335, 36423, 36450, 36481, 38447, 38784, 39387, 39458, 39822, 40305, 40869, 40926, 41010, 41134,

41984, 42172, 42753, 43011, 43176, 43320, 43381, 44142, 44383, 44726, 45087, 45141, 45359, 45421, 45456, 45467, 45486, 45709, 45716, 47626, 49413, 49796, 49962, 50075, 50093, 50571, 50615, 50780, 50851, 51459, 53193, 53702, 53736, 53795, 54109, 54126, 54230, 54894, 55455, 55499, 56522, 56662, 56954, 57267, 58282, 58916, 59544, 59666, 59913, 66846, 67245, 67652, 67955, 67966, 68420, 70226, 70810, 72246, 73330, 73457, 74389, 74638, 74640, 75358, 75952, 76098, 77836, 78449, 78507, 80031, 81695, 82775, 82795, 84611, 84657, 84693, 85020, 85048, 85100, 85325, 85452, 85868, 85936, 85990, 86139, 86497, 87236, 87248, 87533, 87912, 88108, 88494, 89598, 90235, 91287, 91359, 92384, 92410, 92900, 94495, 94512, 97777 and 98333.

14. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 4 selected from the group consisting of 1673, 20577, 33137, 39822, 45716, 49962, 51459, 54894, 55455, 55499, 58282, 68420 and 80031.

15. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in linkage disequilibrium with one or more positions in claim 4, 7, 10 or 13.

16. The method of claim 1, wherein detecting the presence or absence of the one or more polymorphic variations comprises:

hybridizing an oligonucleotide to the nucleic acid sample, wherein the oligonucleotide is complementary to a nucleotide sequence in the nucleic acid and hybridizes to a region adjacent to the polymorphic variation;

extending the oligonucleotide in the presence of one or more nucleotides, yielding extension products; and

detecting the presence or absence of a polymorphic variation in the extension products.

17. The method of claim 1, wherein the subject is a human.

18. The method of claim 17, wherein the subject is a human female.

19. The method of claim 17, wherein the subject is a human male.

20. A method for identifying a polymorphic variation associated with osteoarthritis proximal to an incident polymorphic variation associated with osteoarthritis, which comprises:

identifying a polymorphic variation proximal to the incident polymorphic variation associated with osteoarthritis, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-12;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation;

determining the presence or absence of an association of the proximal polymorphic variant with osteoarthritis.

21. The method of claim 20, wherein the incident polymorphic variation is at one or more positions in claim 4, 7, 10 or 13.

22. The method of claim 20, wherein the proximal polymorphic variation is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the incident polymorphic variation.

23. The method of claim 20, which further comprises determining whether the proximal polymorphic variation is in linkage disequilibrium with the incident polymorphic variation.

24. The method of claim 20, which further comprises identifying a second polymorphic variation proximal to the identified proximal polymorphic variation associated with osteoarthritis and determining if the second proximal polymorphic variation is associated with osteoarthritis.

25. The method of claim 24, wherein the second proximal polymorphic variant is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the proximal polymorphic variation associated with osteoarthritis.

26. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-12;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation; and

(e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);

wherein the nucleotide sequence comprises a polymorphic variation associated with osteoarthritis selected from the group consisting of in SEQ ID NO: 1 a thymine at position 229, a guanine at position 6310, a thymine at position 16559, an adenine at position 18453, an adenine at position 25504, an adenine at position 27174, an adenine at position 30832, a guanine at position 44850, an adenine at position 45884, an adenine at position 48589, a cytosine at position 61477, a cytosine at position 82961 and a thymine at position 46252; in SEQ ID NO: 2 a cytosine at position 40985, a guanine at position 46168, a thymine at position 51925 and a cytosine at position 52168; in SEQ ID NO: 3 a guanine at position 15111, a thymine at position 45641, an adenine at position 46059, a cytosine at position 49693, an adenine at position 49874, an adenine at position 50020, a guanine at position 50719, an adenine at position 70529, an adenine at position 82475, a thymine at position 92462, a thymine at position 92480 and a cytosine at position 96275; and in SEQ ID NO: 4 a guanine at position 1673, a thymine at position 20577, a guanine at position 33137, a guanine at position 39822, an adenine at position 45716, a guanine at position 49962, an adenine at position 51459, a cytosine at position 54894, an adenine at position 55455, an adenine at position 55499, a guanine at position 58282, an adenine at position 68420 and a thymine at position 80031.

27. An oligonucleotide comprising a nucleotide sequence complementary to a portion of the nucleotide sequence of (a), (b), (c), or (d) in claim 26, wherein the 3' end of the oligonucleotide is adjacent to a polymorphic variation associated with osteoarthritis.

28. A microarray comprising an isolated nucleic acid of claim 26 linked to a solid support.

29. An isolated polypeptide encoded by the isolated nucleic acid sequence of claim 26.

30. A method for identifying a candidate therapeutic for treating osteoarthritis, which comprises:

(a) introducing a test molecule to a system which comprises a nucleic acid comprising a nucleotide sequence selected from the group consisting of:

(i) a nucleotide sequence in SEQ ID NO: 1-12;

(ii) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(iv) a fragment of a nucleotide sequence of (a), (b), or (c); or

introducing a test molecule to a system which comprises a protein encoded by a nucleotide sequence of (i), (ii), (iii), or (iv); and

(b) determining the presence or absence of an interaction between the test molecule and the nucleic acid or protein,

whereby the presence of an interaction between the test molecule and the nucleic acid or protein identifies the test molecule as a candidate therapeutic for treating osteoarthritis.

31. The method of claim 30, wherein the system is an animal.

32. The method of claim 30, wherein the system is a cell.

33. The method of claim 30, wherein the nucleotide sequence comprises one or more polymorphic variations associated with osteoarthritis.

34. The method of claim 33, wherein the one or more polymorphic variations associated with osteoarthritis are at one or more positions in claim 4, 7, 10 or 13.

35. A method for treating osteoarthritis in a subject, which comprises contacting one or more cells of a subject in need thereof with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-12;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(d) a fragment of a nucleotide sequence of (a), (b), or (c); and

(e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);

whereby contacting the one or more cells of the subject with the nucleic acid treats the osteoarthritis in the subject.

36. The method of claim 35, wherein the nucleic acid is RNA or PNA.

37. The method of claim 36, wherein the nucleic acid is duplex RNA.

38. A method for treating osteoarthritis in a subject, which comprises contacting one or more cells of a subject in need thereof with a protein, wherein the protein is encoded by a nucleotide sequence which comprises a polynucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-12;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(d) a fragment of a nucleotide sequence of (a), (b), or (c);

whereby contacting the one or more cells of the subject with the protein treats the osteoarthritis in the subject.

39. A method for treating osteoarthritis in a subject, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in a nucleic acid sample from a subject, wherein the one or more polymorphic variation are detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-12;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation; and

administering an osteoarthritis treatment to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

40. The method of claim 39, wherein the one or more polymorphic variations are detected at one or more positions in claim 4, 7, 10 or 13.

41. The method of claim 39, wherein the treatment is selected from the group consisting of administering a corticosteroid, a nonsteroidal anti-inflammatory drug (NSAID), a cyclooxygenase-2 (COX-2) inhibitor, an antibody, a glucocorticoid, hyaluronic acid, chondrotin sulfate, glucosamine or acetaminophen; prescribing a heat/cold regimen or a joint protection regimen; performing joint surgery; prescribing a weight control regimen; and combinations of the foregoing.

42. A method for detecting or preventing osteoarthritis in a subject, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-12;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation; and

administering an osteoarthritis prevention or detection procedure to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

43. The method of claim 42, wherein the one or more polymorphic variations are detected at one or more positions in claim 4, 7, 10 or 13.

44. The method of claim 42, wherein the osteoarthritis prevention is selected from the group consisting of administering a corticosteroid, a nonsteroidal anti-inflammatory drug (NSAID), a cyclooxygenase-2 (COX-2) inhibitor, an antibody, a glucocorticoid, hyaluronic acid, chondrotin sulfate, glucosamine or acetaminophen; prescribing a heat/cold regimen or a joint protection regimen; performing joint surgery; prescribing a weight control regimen; and combinations of the foregoing.

45. A method of targeting information for preventing or treating osteoarthritis to a subject in need thereof, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-12;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-12;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation; and

directing information for preventing or treating osteoarthritis to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

46. The method of claim 45, wherein the one or more polymorphic variations are detected at one or more positions in claim 4, 7, 10 or 13.

47. A composition comprising a cell from a subject having osteoarthritis or at risk of osteoarthritis and an antibody that specifically binds to a protein, polypeptide or peptide encoded by a nucleotide sequence identical to or 90% or more identical to a nucleotide sequence in SEQ ID NO: 1-12.

48. A composition comprising a cell from a subject having osteoarthritis or at risk of osteoarthritis and a RNA, DNA, PNA or ribozyme molecule comprising a nucleotide sequence identical to or 90% or more identical to a portion of a nucleotide sequence in SEQ ID NO: 1-12.

49. The composition of claim 48, wherein the RNA molecule is a short inhibitory RNA molecule.

Abstract of the Disclosure

Provided herein are methods for identifying a risk of osteoarthritis in a subject, reagents and kits for carrying out the methods, methods for identifying candidate therapeutics for treating osteoarthritis, and therapeutic and preventative methods applicable to osteoarthritis. These embodiments are based upon an analysis of polymorphic variations in nucleotide sequences within the human genome.

FIGURE 1A

CHROM 6 – DISCOVERY P-VALUES (female only)

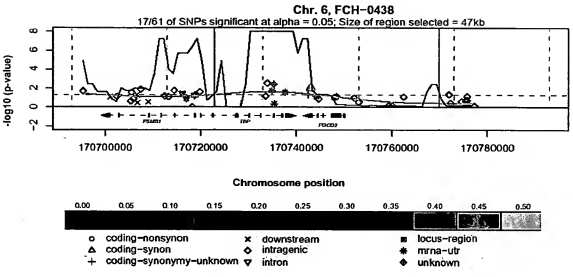


FIGURE 1B

ELP3 – DISCOVERY P-VALUES (female only)

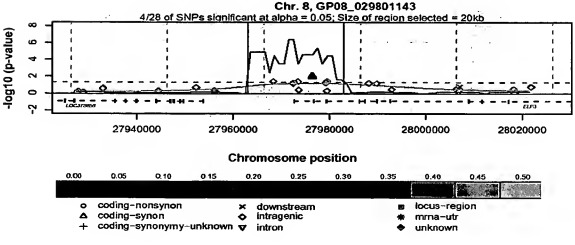


FIGURE 1C

CHDC1 – DISCOVERY P-VALUES (female only)

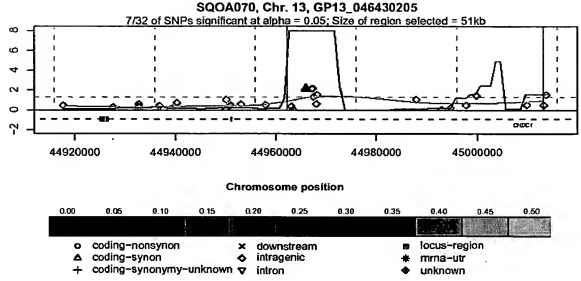
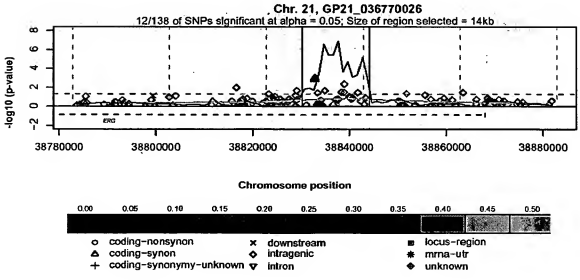


FIGURE 1D

ERG – DISCOVERY P-VALUES (female only)



Application Data Sheet

Application Information

Application Type::	Provisional
Subject Matter::	Utility
Suggested Group Art Unit::	Not Yet Assigned
CD-ROM or CD-R?::	None
Sequence submission?::	None
Computer Readable Form (CRF)?::	No
Title::	METHODS FOR IDENTIFYING RISK OF OSTEOARTHRITIS AND TREATMENTS THEREOF
Attorney Docket Number::	524593008700
Request for Early Publication?::	No
Request for Non-Publication?::	No
Total Drawing Sheets?::	2
Small Entity?::	Yes
Petition included?::	No
Secrecy Order in Parent Appl.?::	No

Applicant Information

Applicant Authority Type::	Inventor
Primary Citizenship Country::	US
Status::	Full Capacity
Given Name::	Steven
Family Name::	MAH
City of Residence::	San Diego
State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	12820 Via Nieve #74
City of mailing address::	San Diego
State or Province of mailing address::	CA

Postal or Zip Code of mailing address::	92130

Applicant Authority Type::	Inventor
Primary Citizenship Country::	Germany
Status::	Full Capacity
Given Name::	Andreas
Family Name::	BRAUN
City of Residence::	San Diego
State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	3935 Lago Di Grata Circle
City of mailing address::	San Diego
State or Province of mailing address::	CA
Postal or Zip Code of mailing address::	92130

Applicant Authority Type::	Inventor
Primary Citizenship Country::	Germany
Status::	Full Capacity
Given Name::	Stefan
Middle Name::	M.
Family Name::	KAMMERER
City of Residence::	San Diego
State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	3825 Elijah Court, Unit 334
City of mailing address::	San Diego
State or Province of mailing address::	CA
Postal or Zip Code of mailing address::	92130

Applicant Authority Type::	Inventor
Primary Citizenship Country::	US
Status::	Full Capacity

Given Name::	Matthew
Middle Name::	Roberts
Family Name::	NELSON
City of Residence::	San Marcos
State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	1250 Calle Prospero
City of mailing address::	San Marcos
State or Province of mailing address::	CA
Postal or Zip Code of mailing address::	92069

Applicant Authority Type::	Inventor
Primary Citizenship Country::	Sweden
Status::	Full Capacity
Given Name::	Rikard
Middle Name::	Henry
Family Name::	RENELAND
City of Residence::	San Diego
State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	7555 Charmant Drive, #1114
City of mailing address::	San Diego
State or Province of mailing address::	CA
Postal or Zip Code of mailing address::	92122

Applicant Authority Type::	Inventor
Primary Citizenship Country::	United Kingdom
Status::	Full Capacity
Given Name::	Maria
Middle Name::	L.
Family Name::	LANGDOWN
City of Residence::	San Diego

State or Province of Residence::	CA
Country of Residence::	US
Street of mailing address::	3701 Yosemite Street
City of mailing address::	San Diego
State or Province of mailing address::	CA
Postal or Zip Code of mailing address::	92109

Correspondence Information

Correspondence Customer Number::	25225

Representative Information

Representative Customer Number::	25225